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FILE COVERS 1907 - 10 Jun 2005  VOL 142 ISS 25
FILE LAST UPDATED: 9 Jun 2005  (20050609/ED)

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  substance identification.

=> d que
L1            59 SEA FILE=CAPLUS LANSOPRAZOLE AND STABLE
L2            23 SEA FILE=CAPLUS L1 AND WATER


=> d l2 1-23 ibib abs hit

L2   ANSWER 1 OF 23  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2005:281759  CAPLUS
DOCUMENT NUMBER:          142:341903
TITLE:                    Pharmaceutical compositions of benzimidazole and
                          processes for their preparation
INVENTOR(S):              Singh, Romi Barat; Kumar, Pananchukunnath Manoj;
                          Nagaprasad, Vishnubhotla; Sethi, Sanjeev Kumar; Malik,
                          Rajiv
PATENT ASSIGNEE(S):       Ranbaxy Laboratories Limited, India
SOURCE:                   PCT Int. Appl., 21 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2005027876         A1    20050331    WO 2004-IB2784          20040827
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
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WO 2004075881 A1 20040910 WO 2004-IB536 20040301
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: IN 2003-DE1047 A 20030828
WO 2004-IB536 A 20040301
IN 2003-DE203 A 20030228

AB The tech. field of the present invention relates to **stable** pharmaceutical compns. of acid-labile benzimidazole derivative using increased amts. of low-viscosity hydroxypropylcellulose, and processes for the preparation of these compns. The pharmaceutical composition includes one or more cores. The cores include an acid-labile benzimidazole derivative and at least 10% weight/weight of low-viscosity hydroxypropylcellulose by weight of the benzimidazole derivative

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The tech. field of the present invention relates to **stable** pharmaceutical compns. of acid-labile benzimidazole derivative using increased amts. of low-viscosity hydroxypropylcellulose, and processes for the preparation of these compns. The pharmaceutical composition includes one or more cores. The cores include an acid-labile benzimidazole derivative and at least 10% weight/weight of low-viscosity hydroxypropylcellulose by weight of the benzimidazole derivative

IT 51-17-2D, Benzimidazole, derivs. 73590-58-6, Omeprazole 102625-70-7, Pantoprazole 103577-45-3, **Lansoprazole** 104340-86-5, Leminoprazole 117976-89-3, Rabeprazole 117976-90-6, Pariprazole 119141-88-7, Esomeprazole 138786-67-1, Pantoprazole sodium
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pharmaceutical compns. of benzimidazole)

IT 67-56-1, Methanol, uses 67-63-0, Isopropyl alcohol, uses 67-64-1, Acetone, uses 75-09-2, Methylene chloride, uses 7732-18-5, **Water**, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; pharmaceutical compns. of benzimidazole)

L2 ANSWER 2 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1005301 CAPLUS
DOCUMENT NUMBER: 142:246134
TITLE: Method of making oral preparation of omeprazole
INVENTOR(S): Hong, Seok Cheon; Kil, Yeong Sik
PATENT ASSIGNEE(S): Korea United Pharm. Inc., S. Korea
SOURCE: Repub. Korean Kongkae Taeho Kongbo, No pp. given
CODEN: KRXXA7
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

KR 2003039707	A	20030522	KR 2001-70733	20011114

PRIORITY APPLN. INFO.: KR 2001-70733 20011114

AB An oral preparation containing omeprazole is provided which is pharmaceutically **stable** by prevention of the loss of activity of omeprazole caused by gastric acid when orally administered and facilitating the absorption thereof into the small intestine, thereby maximizing therapeutic effect. In a method of making an oral preparation, non-volatile minute granules with a particle size of 0.2-0.7 mm are first made using starch and sugar, or only sugar. Then, omeprazole or **lansoprazole** and the salt thereof, and a binder selected from hydroxy Pr Me cellulose or hydroxy Pr cellulose and derivs. thereof are dissolved or diffused in a solvent containing a mixture of purified **water**, acetone and ethanol. The resulting solution, and the minute granules are mixed together with talc. The mixture is coated by a protection film to produce a pellet having a diameter of 0.3-2.5 mm.

AB An oral preparation containing omeprazole is provided which is pharmaceutically **stable** by prevention of the loss of activity of omeprazole caused by gastric acid when orally administered and facilitating the absorption thereof into the small intestine, thereby maximizing therapeutic effect. In a method of making an oral preparation, non-volatile minute granules with a particle size of 0.2-0.7 mm are first made using starch and sugar, or only sugar. Then, omeprazole or **lansoprazole** and the salt thereof, and a binder selected from hydroxy Pr Me cellulose or hydroxy Pr cellulose and derivs. thereof are dissolved or diffused in a solvent containing a mixture of purified **water**, acetone and ethanol. The resulting solution, and the minute granules are mixed together with talc. The mixture is coated by a protection film to produce a pellet having a diameter of 0.3-2.5 mm.

IT 9004-64-2, Hydroxy propyl cellulose 9004-65-3, Hydroxy propyl methyl cellulose 14807-96-6, Talc, biological studies 73590-58-6, Omeprazole 103577-45-3, **Lansoprazole**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(making oral preparation of omeprazole)

L2 ANSWER 3 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:878281 CAPLUS
DOCUMENT NUMBER: 141:355384
TITLE: A **stable** oral benzimidazole formulation
INVENTOR(S): Desai, Jatin; Patel, Pankaj Ramanbhai; Veerababu, Ramabrahammam T.; Jogani, Pranav
PATENT ASSIGNEE(S): Cadila Healthcare Limited, India
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089333	A2	20041021	WO 2004-IN50	20040226
WO 2004089333	A3	20050203		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IN 2003-MU237 A 20030228

AB A **stable** oral pharmaceutical composition comprising a benzimidazole compound or its pharmaceutically acceptable salt is described, wherein the active ingredient is coated with an enteric coating polymer and has no separating or protective layer in between. These pellets can be filled into the capsules or compressed into tablets. Further, a method for the manufacture of such a formulation, and the use of such a formulation in medicine is disclosed. For example, sugar beads (1000 g) were coated with a composition containing omeprazole 200 g, hydroxypropyl Me cellulose 240 g, talc 200 g, and **water** as needed to form pellets. Pellets (500 g) were then enteric coated with a composition containing Eudragit L30D-55 690 g, tri-Et citrate 19.15 g, talc 24.24 g, 30% ammonia solution as needed for pH 4.5 to 5.5, and **water** as needed. The coated pellets can be filled in hard gelatin capsules. When tested 99.3 to 100% drug was released within 30 min. The unit dose pellets contained less than 0.7% related substances. The gastro-resistance was found to be 1.81%.

TI A **stable** oral benzimidazole formulation

AB A **stable** oral pharmaceutical composition comprising a benzimidazole compound or its pharmaceutically acceptable salt is described, wherein the active ingredient is coated with an enteric coating polymer and has no separating or protective layer in between. These pellets can be filled into the capsules or compressed into tablets. Further, a method for the manufacture of such a formulation, and the use of such a formulation in medicine is disclosed. For example, sugar beads (1000 g) were coated with a composition containing omeprazole 200 g, hydroxypropyl Me cellulose 240 g, talc 200 g, and **water** as needed to form pellets. Pellets (500 g) were then enteric coated with a composition containing Eudragit L30D-55 690 g, tri-Et citrate 19.15 g, talc 24.24 g, 30% ammonia solution as needed for pH 4.5 to 5.5, and **water** as needed. The coated pellets can be filled in hard gelatin capsules. When tested 99.3 to 100% drug was released within 30 min. The unit dose pellets contained less than 0.7% related substances. The gastro-resistance was found to be 1.81%.

IT Glycerides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C12-18, polymers with ethylene glycol; preparation of **stable** benzimidazole enteric-coated oral formulations)

IT Monoglycerides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C18-unsatd., polymers with ethylene glycol; preparation of **stable** benzimidazole enteric-coated oral formulations)

IT Glycerides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C8-10, ethoxylated, solubilizer; preparation of **stable** benzimidazole enteric-coated oral formulations)

IT Carbohydrates, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(beads, cores; preparation of **stable** benzimidazole enteric-coated oral formulations)

IT Drug delivery systems
(capsules, enteric-coated; preparation of **stable** benzimidazole enteric-coated oral formulations)

IT Castor oil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ethoxylated, Cremophore EL, solubilizer; preparation of **stable** benzimidazole enteric-coated oral formulations)

IT Glycerides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medium-chain, solubilizer; preparation of **stable** benzimidazole enteric-coated oral formulations)

IT Drug delivery systems
(pellets, enteric-coated; preparation of **stable** benzimidazole

enteric-coated oral formulations)
IT Gums and Mucilages
Plasticizers
Solubilizers
(preparation of **stable** benzimidazole enteric-coated oral formulations)
IT Glycerides, biological studies
Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of **stable** benzimidazole enteric-coated oral formulations)
IT Drug delivery systems
(tablets, enteric-coated; preparation of **stable** benzimidazole enteric-coated oral formulations)
IT 9003-39-8D, crosslinked
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Crospovidone; preparation of **stable** benzimidazole enteric-coated oral formulations)
IT 9005-25-8, Starch, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cores; preparation of **stable** benzimidazole enteric-coated oral formulations)
IT 79-41-4D, Methacrylic acid, esters, polymers 9004-38-0, Cellulose acetate phthalate 9010-88-2, Ethyl acrylate-methyl methacrylate copolymer 9050-31-1, Hydroxypropyl methyl cellulose phthalate 25212-88-8, Eudragit L30D-55 37205-99-5, Carboxymethyl ethyl cellulose 53237-50-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enteric coating; preparation of **stable** benzimidazole enteric-coated oral formulations)
IT 9004-34-6, Cellulose, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microcryst., cores; preparation of **stable** benzimidazole enteric-coated oral formulations)
IT 77-93-0, Triethyl citrate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(plasticizer; preparation of **stable** benzimidazole enteric-coated oral formulations)
IT 51-17-2D, Benzimidazole, compds. 57-50-1, Sucrose, biological studies 4070-80-8, Sodium stearyl fumarate 9003-39-8, Polyvinylpyrrolidone 9004-32-4, Carboxymethyl cellulose sodium 9004-64-2, Hydroxypropyl cellulose 9004-65-3, Hydroxypropyl methyl cellulose 9005-65-6, Tween 80 25322-68-3, Polyethylene glycol 31566-31-1, Glyceryl monostearate 73590-58-6, Omeprazole 102625-70-7, Pantoprazole 103577-45-3, **Lansoprazole** 117976-89-3, Rabeprazole
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of **stable** benzimidazole enteric-coated oral formulations)
IT 151-21-3, Sodium lauryl sulfate, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solubilizer; preparation of **stable** benzimidazole enteric-coated oral formulations)

L2 ANSWER 4 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:834106 CAPLUS
DOCUMENT NUMBER: 142:397408
TITLE: Preparation and evaluation of inclusion complex of **lansoprazole** with 2-HP-β-cyclodextrin and meglumine
AUTHOR(S): Lee, Jung Woo; Kim, Jung Su; Chang, Hye Jin; Lee, Gye Won; Jee, Ung Kil
CORPORATE SOURCE: College of Pharmacy, Chungnam National University,

Daejeon, 305-764, S. Korea
SOURCE: Yakche Hakhoechi (2004), 34(4), 269-274
CODEN: YAHAEX; ISSN: 0259-2347
PUBLISHER: Korean Society of Pharmaceutics
DOCUMENT TYPE: Journal
LANGUAGE: Korean

AB To enhance the solubility and stability of **lansoprazole** (LAN), new proton pump inhibitor, we were prepared various molar ratio of inclusion complex with 2-hydroxypropyl-β-cyclodextrin (HPCD) and organic alkali agent, meglumine (MEG). Inclusion complex formation of LAN with HPCD was investigated by Differential Scanning Calorimetry and X-ray diffractometry. The aqueous solubilities of inclusion complexes, and the stabilities of 1:4 and 1:5 inclusion complexes in aqueous solns. containing different concns. of MEG were examined The stability of 1:5 LAN-HPCD inclusion complex containing MEG, which was equaled to amount of LAN, was performed in 0.9% NaCl and 5% dextrose solution The formation of inclusion complex of LAN with HPCD was AL type and the molar ratio of complex was 1:1. The stability constant was 41.557 M-1. As molar ratio of LAN to HPCD was increased, solubility of inclusion complex was increased. 1:5 LAN-HPCD inclusion complex was more **stable** than 1:4 LAN-HPCD inclusion complex. And as contained MEG amount in LAN solution was increased, stability of 1:4 and 1:5 LAN-HPCD inclusion complexes was improved. Also stability of 1:5 LAN-HPCD-MEG inclusion complex in 0.9% NaCl solution and 5% dextrose solution was similar to it in **water** at room temperature, but it was unstable at 40°C.

TI Preparation and evaluation of inclusion complex of **lansoprazole** with 2-HP-β-cyclodextrin and meglumine

AB To enhance the solubility and stability of **lansoprazole** (LAN), new proton pump inhibitor, we were prepared various molar ratio of inclusion complex with 2-hydroxypropyl-β-cyclodextrin (HPCD) and organic alkali agent, meglumine (MEG). Inclusion complex formation of LAN with HPCD was investigated by Differential Scanning Calorimetry and X-ray diffractometry. The aqueous solubilities of inclusion complexes, and the stabilities of 1:4 and 1:5 inclusion complexes in aqueous solns. containing different concns. of MEG were examined The stability of 1:5 LAN-HPCD inclusion complex containing MEG, which was equaled to amount of LAN, was performed in 0.9% NaCl and 5% dextrose solution The formation of inclusion complex of LAN with HPCD was AL type and the molar ratio of complex was 1:1. The stability constant was 41.557 M-1. As molar ratio of LAN to HPCD was increased, solubility of inclusion complex was increased. 1:5 LAN-HPCD inclusion complex was more **stable** than 1:4 LAN-HPCD inclusion complex. And as contained MEG amount in LAN solution was increased, stability of 1:4 and 1:5 LAN-HPCD inclusion complexes was improved. Also stability of 1:5 LAN-HPCD-MEG inclusion complex in 0.9% NaCl solution and 5% dextrose solution was similar to it in **water** at room temperature, but it was unstable at 40°C.

ST **lansoprazole** hydroxypropyl cyclodextrin inclusion complex meglumine soly

IT Drug delivery systems
(solns.; preparation and evaluation of inclusion complex of **lansoprazole** with 2-HP-β-cyclodextrin and meglumine)

IT 57-55-6DP, 1,2-Propanediol, cyclodextrin ethers, **lansoprazole** complexes 7585-39-9DP, β-Cyclodextrin, hydroxypropyl ethers, **lansoprazole** complexes 103577-45-3DP, **Lansoprazole**, complexes with hydroxypropyl cyclodextrin
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and evaluation of inclusion complex of **lansoprazole** with 2-HP-β-cyclodextrin and meglumine)

IT 6284-40-8, Meglumine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation and evaluation of inclusion complex of **lansoprazole**

with 2-HP-β-cyclodextrin and meglumine)

L2 ANSWER 5 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:696366 CAPLUS
DOCUMENT NUMBER: 141:212763
TITLE: Method of stabilizing **lansoprazole**
INVENTOR(S): Singer, Claude; Liberman, Anita; Veinberg, Irena
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals Usa, Inc.
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004072061	A1	20040826	WO 2004-US3603	20040205
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1485373	A1	20041215	EP 2004-708666	20040205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005020638	A1	20050127	US 2004-773535	20040205
PRIORITY APPLN. INFO.:			US 2003-445219P P	20030205
			WO 2004-US3603 W	20040205

AB The present invention provides a **stable** 2-(2-pyridylmethyl)sulfinyl-1H-benzimidazole (**lansoprazole**) and a method for stabilizing **lansoprazole** by use of a weakly basic material. The present invention also provides a method for the preparation of a **stable lansoprazole**. **Lansoprazole** was prepared by oxidation its thio analog and purified with a solution of EtOH, NH3, and **water**.

TI Method of stabilizing **lansoprazole**

AB The present invention provides a **stable** 2-(2-pyridylmethyl)sulfinyl-1H-benzimidazole (**lansoprazole**) and a method for stabilizing **lansoprazole** by use of a weakly basic material. The present invention also provides a method for the preparation of a **stable lansoprazole**. **Lansoprazole** was prepared by oxidation its thio analog and purified with a solution of EtOH, NH3, and **water**.

ST **lansoprazole** stabilization purifn prepn

IT Crystallization
(stabilizing **lansoprazole**)

IT Acids, processes
Amines, processes
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)
(stabilizing **lansoprazole**)

IT 131926-99-3P, 1H-Benzimidazole, 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]sulfonyl-
RL: BYP (Byproduct); PREP (Preparation)
(stabilizing **lansoprazole**)

IT 64-17-5, Ethanol, processes 64-18-6, Formic acid, processes 64-19-7, Acetic acid, processes 67-56-1, Methanol, processes 67-63-0, 2-Propanol, processes 67-64-1, Acetone, processes 68-12-2, Dmf, processes 71-23-8, 1-Propanol, processes 74-89-5, Methylamine, processes 78-93-3, 2-Butanone, processes 102-71-6, Triethanolamine, processes 109-89-7, Diethylamine, processes 109-99-9, Thf, processes 111-42-2, Diethanolamine, processes 121-44-8, Triethylamine, processes 1336-21-6, Ammonium hydroxide 7647-01-0, Hydrochloric acid, processes 7664-41-7, Ammonia, processes
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)
(stabilizing **lansoprazole**)

IT 103577-45-3P, **Lansoprazole**
RL: PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(stabilizing **lansoprazole**)

IT 103577-40-8, 1H-Benzimidazole, 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]thio-
RL: RCT (Reactant); RACT (Reactant or reagent)
(stabilizing **lansoprazole**)

L2 ANSWER 6 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:648368 CAPLUS
DOCUMENT NUMBER: 141:179632
TITLE: **Stable** oral benzimidazole compositions
INVENTOR(S): Mehta, Kamal; Mathur, Rajeev Shanker; Sethi, Sanjeev Kumar; Malik, Rajiv; Gandhi, Rajesh; Isloor, Shashikanth; Malik, Rajiv
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004066982	A1	20040812	WO 2004-IB235	20040202

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI

PRIORITY APPLN. INFO.: IN 2003-DE80 A 20030131
IN 2003-DE728 A 20030527

AB The present invention relates to **stable** oral benzimidazole compns. and processes for their preparation The **stable** oral benzimidazole pharmaceutical composition includes a core, a separating layer, and an enteric coating. The core includes a benzimidazole compound, a substantially **water**-soluble material and, optionally excipients, wherein the core is not alkaline The separating layer surrounds the core and includes a substantially **water**-soluble material and, excipients. The enteric coating surrounds the separating layer. At least one of the core

and the separating layer includes the substantially **water**-soluble material without any excipients. Thus, an enteric coating comprised Eudragit L30D55 114.39, PEG-300 3.43, talc 12.12, TiO2 4.04 mg and **water** qs.

TI **Stable** oral benzimidazole compositions

AB The present invention relates to **stable** oral benzimidazole compns. and processes for their preparation The **stable** oral benzimidazole pharmaceutical composition includes a core, a separating layer, and an enteric coating. The core includes a benzimidazole compound, a substantially **water**-soluble material and, optionally excipients, wherein the core is not alkaline The separating layer surrounds the core and includes a substantially **water**-soluble material and, excipients. The enteric coating surrounds the separating layer. At least one of the core and the separating layer includes the substantially **water**-soluble material without any excipients. Thus, an enteric coating comprised Eudragit L30D55 114.39, PEG-300 3.43, talc 12.12, TiO2 4.04 mg and **water** qs.

ST **Stable** oral benzimidazole pharmaceutical

IT Drug delivery systems
(capsules, enteric-coated; **stable** oral benzimidazole compns.)

IT Drug delivery systems
(enteric-coated; **stable** oral benzimidazole compns.)

IT Drug delivery systems
(oral; **stable** oral benzimidazole compns.)

IT Binders
Gums and Mucilages
Lubricants
(**stable** oral benzimidazole compns.)

IT Alditols
Carbohydrates, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** oral benzimidazole compns.)

IT Drug delivery systems
(tablets, enteric-coated; **stable** oral benzimidazole compns.)

IT Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**water**-soluble; **stable** oral benzimidazole compns.)

IT 9004-34-6, Cellulose, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microcryst.; **stable** oral benzimidazole compns.)

IT 50-70-4, Sorbitol, biological studies 50-99-7, Dextrose, biological studies 57-50-1, Sucrose, biological studies 63-42-3, Lactose 69-65-8, Mannitol 87-99-0, Xylitol 557-04-0 4070-80-8, Sodium stearyl fumarate 7631-86-9, Silica, biological studies 9000-01-5, Gum arabic 9000-65-1, Gum tragacanth 9003-39-8, Polyvinylpyrrolidone 9004-34-6D, Cellulose, derivs. 9004-64-2, Hydroxypropyl cellulose 9004-65-3, Hydroxypropyl methyl cellulose 9004-67-5 9005-25-8, Starch, biological studies 9005-25-8D, Starch, derivs. 9063-38-1, Sodium starch glycolate 11138-66-2, Xanthan gum 14807-96-6, Talc, biological studies 25086-89-9, Vinyl acetate-vinylpyrrolidone copolymer 25212-88-8, Eudragit L30D 55 73590-58-6, Omeprazole 74811-65-7, Croscarmellose sodium 102625-70-7, Pantoprazole 103577-45-3, **Lansoprazole** 117976-89-3, Rabeprazole 198085-73-3, Pearlitol SD 200 444902-50-5, Acryl-Eze
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** oral benzimidazole compns.)

L2 ANSWER 7 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:453207 CAPLUS
DOCUMENT NUMBER: 141:12318
TITLE: **Stable lansoprazole** containing

more than 500-3000 ppm **water** and 200-5000 ppm alcohol

INVENTOR(S): Singer, Claude; Liberman, Anita; Veinberg, Irena

PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.

SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004046135	A1	20040603	WO 2003-US37164		20031118
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
EP 1465890	A1	20041013	EP 2003-789888		20031118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
US 2004215021	A1	20041028	US 2003-717325		20031118
PRIORITY APPLN. INFO.:			US 2002-427589P	P	20021118
			US 2003-445219P	P	20030205
			WO 2003-US37164	W	20031118

AB The present invention provides a **stable lansoprazole** comprising either 500-3000 ppm **water** and 200-5000 ppm alc., or both. The present invention provides a method of preparing a **stable lansoprazole** as well as a pharmaceutical composition containing same. The present invention further provides a method of purifying **lansoprazole** that is substantially free of sulfone and sulfide derivs.

TI **Stable lansoprazole** containing more than 500-3000 ppm **water** and 200-5000 ppm alcohol

AB The present invention provides a **stable lansoprazole** comprising either 500-3000 ppm **water** and 200-5000 ppm alc., or both. The present invention provides a method of preparing a **stable lansoprazole** as well as a pharmaceutical composition containing same. The present invention further provides a method of purifying **lansoprazole** that is substantially free of sulfone and sulfide derivs.

ST **lansoprazole** compn **stable water** alc

IT Crystallization
Drug delivery systems
(**stable lansoprazole** containing more than 500-3000 ppm **water** and 200-5000 ppm alc.)

IT Drug delivery systems
(tablets; **stable lansoprazole** containing more than 500-3000 ppm **water** and 200-5000 ppm alc.)

IT 7732-18-5, **Water**, uses
RL: NUU (Other use, unclassified); USES (Uses)
(**stable lansoprazole** containing more than 500-3000 ppm **water** and 200-5000 ppm alc.)

IT 64-17-5, Ethanol, uses
RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical

process); PYP (Physical process); PROC (Process); USES (Uses)
(**stable lansoprazole** containing more than 500-3000 ppm **water** and 200-5000 ppm alc.)

IT 103577-45-3, **Lansoprazole**
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**stable lansoprazole** containing more than 500-3000 ppm **water** and 200-5000 ppm alc.)

IT 64-18-6, Formic acid, processes 64-19-7, Acetic acid, processes 67-56-1, Methanol, processes 67-63-0, 2-Propanol, processes 67-64-1, Acetone, processes 68-12-2, Dmf, processes 71-23-8, 1-Propanol, processes 74-89-5, Methylamine, processes 78-93-3, 2-Butanone, processes 102-71-6, Triethanolamine, processes 105-58-8, Diethyl carbonate 109-89-7, Diethylamine, processes 109-99-9, Thf, processes 111-42-2, Diethanolamine, processes 121-44-8, Triethylamine, processes 616-38-6, Dimethyl carbonate 1336-21-6, Ammonium hydroxide 7647-01-0, Hydrochloric acid, processes 7664-41-7, Ammonia, processes
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)
(**stable lansoprazole** containing more than 500-3000 ppm **water** and 200-5000 ppm alc.)

L2 ANSWER 8 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:162580 CAPLUS
DOCUMENT NUMBER: 140:187434
TITLE: A process for manufacture of **stable** oral multiple unit pharmaceutical composition containing benzimidazoles
INVENTOR(S): Antarkar, Amit Krishna; Abdul Sattar Abdul, Javed; Lala Rajendra, Ghanshamlal; Joshi Ketaki, Kishore; Gadkari Parag, Narayan; Thanawala Gaurang, Hasmukhlal; Shah Maya, Janak; Shah Janak, Ramanlal
PATENT ASSIGNEE(S): Themis Laboratories Private Limited, India
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004016242	A2	20040226	WO 2003-IB3514	20030804
WO 2004016242	A3	20040408		
WO 2004016242	C1	20041007		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2496044	AA	20040226	CA 2003-2496044	20030804
EP 1530460	A2	20050518	EP 2003-787961	20030804
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: IN 2002-MU742 A 20020816
WO 2003-IB3514 W 20030804

AB This invention relates to process for manufacture of a **stable**, oral, multiple unit pharmaceutical composition containing high concentration of benzimidazole up to 40% by weight without the use of micronized benzimidazole, disintegrating agent and fillers. Surfactants in these compns. are in enteric polymer layer and not in contact with benzimidazole. Multiple unit pharmaceutical composition of the invention shows min. acid degradation in 0.1 N HCl after 2 h and pH 6.8 buffer release of more than 85% after 45 min. The multiple unit pharmaceutical composition is in the form unagglomerated, uniformly shaped and sized enteric-coated pellets, which are processed continuously or in batches in single equipment such as fluid bed bottom spray processor. The invention involves sequential deposition of alkaline material layer on non-pareil seeds to obtain treated non-pareil seeds, drug layer to obtain drug pellets, sealant polymer layer to obtain sealed pellets, and enteric polymer layer to obtain enteric coated pellets. The enteric-coated pellets obtained are capable of being filled in smallest size capsules for ease of administration and patient acceptance. Enteric-coated pellets contained omeprazole 24.5, non-pareil seeds 32.3, HPMC-E15 7.3, NaOH 3.2, talc 3.7, and **water** qs to 100%.

TI A process for manufacture of **stable** oral multiple unit pharmaceutical composition containing benzimidazoles

AB This invention relates to process for manufacture of a **stable**, oral, multiple unit pharmaceutical composition containing high concentration of benzimidazole up to 40% by weight without the use of micronized benzimidazole, disintegrating agent and fillers. Surfactants in these compns. are in enteric polymer layer and not in contact with benzimidazole. Multiple unit pharmaceutical composition of the invention shows min. acid degradation in 0.1 N HCl after 2 h and pH 6.8 buffer release of more than 85% after 45 min. The multiple unit pharmaceutical composition is in the form unagglomerated, uniformly shaped and sized enteric-coated pellets, which are processed continuously or in batches in single equipment such as fluid bed bottom spray processor. The invention involves sequential deposition of alkaline material layer on non-pareil seeds to obtain treated non-pareil seeds, drug layer to obtain drug pellets, sealant polymer layer to obtain sealed pellets, and enteric polymer layer to obtain enteric coated pellets. The enteric-coated pellets obtained are capable of being filled in smallest size capsules for ease of administration and patient acceptance. Enteric-coated pellets contained omeprazole 24.5, non-pareil seeds 32.3, HPMC-E15 7.3, NaOH 3.2, talc 3.7, and **water** qs to 100%.

IT Drug delivery systems
(capsules; manufacture of **stable** oral multiple unit pharmaceutical compns. containing benzimidazoles)

IT Binders
Dissolution
Drug bioavailability
Drug bioequivalence
Fillers
Human
Plasticizers
Surfactants
(manufacture of **stable** oral multiple unit pharmaceutical compns. containing benzimidazoles)

IT Alkali metal hydroxides
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)
(manufacture of **stable** oral multiple unit pharmaceutical compns. containing benzimidazoles)

IT Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(manufacture of **stable** oral multiple unit pharmaceutical compns. containing benzimidazoles)
IT Drug delivery systems
(oral; manufacture of **stable** oral multiple unit pharmaceutical compns. containing benzimidazoles)
IT Drug delivery systems
(pellets, enteric-coated; manufacture of **stable** oral multiple unit pharmaceutical compns. containing benzimidazoles)
IT Drug delivery systems
(tablets, enteric-coated; manufacture of **stable** oral multiple unit pharmaceutical compns. containing benzimidazoles)
IT 1305-62-0, Calcium hydroxide, processes 1309-42-8, Magnesium hydroxide 1310-58-3, Potassium hydroxide, processes 1310-73-2, Sodium hydroxide, processes 1336-21-6, Ammonium hydroxide
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)
(manufacture of **stable** oral multiple unit pharmaceutical compns. containing benzimidazoles)
IT 51-17-2D, Benzimidazole, derivs. 73590-58-6, Omeprazole 103577-45-3, **Lansoprazole**
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(manufacture of **stable** oral multiple unit pharmaceutical compns. containing benzimidazoles)
IT 79-41-4D, Methacrylic acid, polymers 546-93-0, Magnesium carbonate 7631-86-9, Silicon dioxide, biological studies 9003-39-8, Polyvinylpyrrolidone 9004-32-4, Sodium carboxymethyl cellulose 9004-64-2, Hydroxypropyl cellulose 9004-65-3, Hydroxypropyl methyl cellulose 9004-67-5, Methyl cellulose 14807-96-6, Talc, biological studies 18641-57-1, Glyceryl behenate 31566-31-1, Glyceryl monostearate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(manufacture of **stable** oral multiple unit pharmaceutical compns. containing benzimidazoles)

L2 ANSWER 9 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:119766 CAPLUS
DOCUMENT NUMBER: 140:152014
TITLE: Enteric coated oral pharmaceutical compositions of acid-unstable drugs
INVENTOR(S): Deshpande, Jayant Venkatesh; Gupte, Vandana Sandeep; Kadam, Vaishali Madhukar; Gosar, Chandrakant Thakarsi; Deshmukh, Satish Ramachandra; Gupte, Rajan Vitthal; Tamhankar, Vijay Ramachandra
PATENT ASSIGNEE(S): Kopran Research Laboratories Limited, India
SOURCE: U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004028737	A1	20040212	US 2002-216315	20020812
PRIORITY APPLN. INFO.:			US 2002-216315	20020812

AB Enteric coated **stable** oral pharmaceutical compns. of acid-unstable drugs are described. The enteric coating is a bilayer with a pH gradient across its thickness comprising an inner layer of neutral or near neutral pH 7-7.5 and an outer layer of acidic pH 2-6. The enteric coating is first carried out at neutral or near neutral pH of 7-7.5 to form an inner layer of neutral or near neutral pH and then at acidic pH of

2-6 to form an outer layer of acidic pH. Tablets of the following composition were prepared: omeprazole 10.30, anhydrous lactose 55.00, Mg stearate 1.00, talc 1.00, colloidal silicon dioxide 0.50, microcryst. cellulose 17.00, corn starch 10.00, and Povidone 3.00 mg. The tablets were enteric coated with the following aqueous organic dispersion of enteric coating material at neutral pH 7: methacrylate copolymer type C 0.4, PEG-600 0.04, Polysorbate-80 0.02, titanium dioxide 0.05, and talc 0.165 kg, iso-Pr alc. 4.0 and **Water** 0.375 L.

AB Enteric coated **stable** oral pharmaceutical compns. of acid-unstable drugs are described. The enteric coating is a bilayer with a pH gradient across its thickness comprising an inner layer of neutral or near neutral pH 7-7.5 and an outer layer of acidic pH 2-6. The enteric coating is first carried out at neutral or near neutral pH of 7-7.5 to form an inner layer of neutral or near neutral pH and then at acidic pH of 2-6 to form an outer layer of acidic pH. Tablets of the following composition were prepared: omeprazole 10.30, anhydrous lactose 55.00, Mg stearate 1.00, talc 1.00, colloidal silicon dioxide 0.50, microcryst. cellulose 17.00, corn starch 10.00, and Povidone 3.00 mg. The tablets were enteric coated with the following aqueous organic dispersion of enteric coating material at neutral pH 7: methacrylate copolymer type C 0.4, PEG-600 0.04, Polysorbate-80 0.02, titanium dioxide 0.05, and talc 0.165 kg, iso-Pr alc. 4.0 and **Water** 0.375 L.

IT 51-17-2D, Benzimidazole, derivs. 59-92-7, Levodopa, biological studies 61-32-5, Methicillin 79-41-4D, Methacrylic acid, esters, polymers 114-07-8, Erythromycin 1406-05-9, Penicillin 4697-36-3, Carbenicillin 8049-47-6, Pancreatin 9004-10-8, Insulin, biological studies 20830-75-5, Digoxin 65277-42-1, Ketoconazole 69655-05-6, Didanosine 73590-58-6, Omeprazole 81093-37-0, Pravastatin 84625-61-6, Itraconazole 102625-70-7, Pantoprazole 103577-45-3, **Lansoprazole** 117976-89-3, Rabeprazole
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enteric coated oral pharmaceutical compns. of acid-unstable drugs)

L2 ANSWER 10 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:60341 CAPLUS
DOCUMENT NUMBER: 140:117406
TITLE: Liquid dosage compositions of **stable** nanoparticulate drugs
INVENTOR(S): Bosch, William H.; Hilborn, Matthew R.; Hovey, Douglas C.; Kline, Laura J.; Lee, Robert W.; Pruitt, John D.; Ryde, Niels P.; Ryde, Tuula A.; Xu, Shuqian
PATENT ASSIGNEE(S): Elan Pharma International, Ltd, Ire.
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 16
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004006959	A1	20040122	WO 2003-US22187	20030716
WO 2004006959	C1	20050331		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,

BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
CA 2492488 AA 20040122 CA 2003-2492488 20030716
PRIORITY APPLN. INFO.: US 2002-396530P P 20020716
WO 2003-US22187 W 20030716

AB The present invention relàtes to liquid dosage compns. of **stable** nanoparticulate drugs. The liquid dosage compns. of the invention include osmotically active crystal growth inhibitors that stabilize the nanoparticulate active agents against crystal and particle size growth of the drug. Thus, an aqueous nanoparticulate colloidal dispersion (NCD) comprising drug 32.5 Copovidone 6.5, and dioctyl sodium sulfosuccinate 0.464% by weight was prepared by milling for 3.8 h under high energy milling conditions. The final mean particle size (by weight) of the drug particles was 161 nm. The concentrated NCD was then diluted with preserved **water** and glycerol (the osmotically active crystal growth inhibitor) to 0.5-3.0% drug.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Liquid dosage compositions of **stable** nanoparticulate drugs

AB The present invention relates to liquid dosage compns. of **stable** nanoparticulate drugs. The liquid dosage compns. of the invention include osmotically active crystal growth inhibitors that stabilize the nanoparticulate active agents against crystal and particle size growth of the drug. Thus, an aqueous nanoparticulate colloidal dispersion (NCD) comprising drug 32.5 Copovidone 6.5, and dioctyl sodium sulfosuccinate 0.464% by weight was prepared by milling for 3.8 h under high energy milling conditions. The final mean particle size (by weight) of the drug particles was 161 nm. The concentrated NCD was then diluted with preserved **water** and glycerol (the osmotically active crystal growth inhibitor) to 0.5-3.0% drug.

ST liq dosage **stable** nanoparticulate drug

IT Inflammation
(Crohn's disease; liquid dosage compns. of **stable** nanoparticulate drugs)

IT Intestine, disease
(Crohn's; liquid dosage compns. of **stable** nanoparticulate drugs)

IT Alcohols, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C16-18, ethoxylated; liquid dosage compns. of **stable** nanoparticulate drugs)

IT Alcohols, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C16-18; liquid dosage compns. of **stable** nanoparticulate drugs)

IT Arthritis
(Reiter's syndrome; liquid dosage compns. of **stable** nanoparticulate drugs)

IT Drug delivery systems
(aerosols; liquid dosage compns. of **stable** nanoparticulate drugs)

IT Diagnosis
(agents; liquid dosage compns. of **stable** nanoparticulate drugs)

IT Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkyl group-terminated; liquid dosage compns. of **stable** nanoparticulate drugs)

IT Quaternary ammonium compounds, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkylbenzyldimethyl, chlorides; liquid dosage compns. of **stable** nanoparticulate drugs)

IT Quaternary ammonium compounds, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkyltrimethyl, chlorides; liquid dosage compns. of **stable**

nanoparticulate drugs)
IT Quaternary ammonium compounds, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkyltrimethyl, ethoxylated; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Fats and Glyceridic oils, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(animal, marine; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Inflammation
Spinal column, disease
(ankylosing spondylitis; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Polyethers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aromatic, sulfonates; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Heart, disease
(arrhythmia; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Skin preparations (pharmaceutical)
(astringents; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Quaternary ammonium compounds, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(benzyl-C12-18-alkyldimethyl, chlorides; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Quaternary ammonium compounds, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(benzyl-C14-18-alkyldimethyl, chlorides; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Drug delivery systems
(bioadhesive; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Drug delivery systems
(buccal; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Joint, anatomical
(bursa, disease, bursitis; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Drug delivery systems
(capsules; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Lipids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cationic; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Uterus, neoplasm
(cervix; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Bronchi, disease
Inflammation
(chronic bronchitis; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Lung, disease
(chronic obstructive; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Quaternary ammonium compounds, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coco alkyl(hydroxyethyl)dimethyl, chlorides; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Quaternary ammonium compounds, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coco alkylbis(hydroxyethyl)methyl, chlorides; liquid dosage compns. of

stable nanoparticulate drugs)
IT Quaternary ammonium compounds, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coco alkyltrimethyl, bromides; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Quaternary ammonium compounds, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coco alkyltrimethyl, chlorides; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Fatty acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coco, esters with sucrose; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Inflammation
Intestine, disease
(colitis; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Imaging agents
(contrast; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Drug delivery systems
(controlled-release; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Mental disorder
(depression; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Quaternary ammonium compounds, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dialkyldimethyl, chlorides; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Tendon
(disease, tendinitis; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Uterus, disease
(endometriosis; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Uterus, neoplasm
(endometrium; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Fatty acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(esters; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Castor oil
Phospholipids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ethoxylated; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Fats and Glyceridic oils, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evening primrose; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Fruit
Vegetable
(exts.; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Heart, disease
(failure; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Intestine, neoplasm
(familial polyposis; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Muscle, disease
(fibromyalgia; liquid dosage compns. of **stable** nanoparticulate

drugs)
IT Inflammation
Stomach, disease
(gastritis; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Digestive tract, disease
Inflammation
(gastroenteritis; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Drug delivery systems
(gels; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Tea products
(green; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Carboxylic acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydroxy; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Animal virus
Eubacteria
Fungi
(infection with; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Lung, disease
(infection; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Intestine, disease
(inflammatory; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Crystal growth
Thyroid gland
(inhibitors; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Drug delivery systems
(injections, i.p.; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Rheumatoid arthritis
(juvenile; liquid dosage compns. of **stable** nanoparticulate drugs)
IT AIDS (disease)
Acne
Adrenoceptor agonists
Allergy
Allergy inhibitors
Aloe barbadensis
Alzheimer's disease
Analgesics
Anorexia
Anthelmintics
Anti-AIDS agents
Anti-Alzheimer's agents
Anti-inflammatory agents
Antiarrhythmics
Antiarthritics
Antiasthmatics
Antibacterial agents
Antibiotics
Anticoagulants
Anticonvulsants
Antidepressants
Antidiabetic agents
Antiemetics
Antihistamines

Antihypertensives
Antimigraine agents
Antiobesity agents
Antioxidants
Antirheumatic agents
Antitumor agents
Antitussives
Antiviral agents
Anxiety
Anxiolytics
Arthritis
Asthma
Blood products
Blood substitutes
Cachexia
Cardiovascular agents
Cardiovascular system, disease
Castration
Cholinergic agonists
Commiphora mukul
Cough
Cystic fibrosis
Diabetes mellitus
Diuresis
Diuretics
Dopamine agonists
Drug bioavailability
Drug bioequivalence
Dysmenorrhea
Dyspepsia
Emphysema
Epilepsy
Fish
Food
Food additives
Food poisoning
Fungicides
Gout
Hemorrhage
Hemostatics
Herb
Hirsutism
Hormone replacement therapy
Human
Hypertension
Hypnotics and Sedatives
Imaging agents
Immunosuppressants
Immunosuppression
Inflammation
Inotropics
Kidney, disease
Kidney, neoplasm
Mammary gland, neoplasm
Motion sickness
Muscarinic antagonists
Muscle contraction
Muscle relaxants
Neoplasm
Obesity
Osteoarthritis
Osteoporosis

Pain
Parathyroid gland
Particle size distribution
Prostate gland, neoplasm
Radiopharmaceuticals
Respiratory distress syndrome
Rheumatoid arthritis
Shear
Size reduction
Sleep
Solubility
Stabilizing agents
Storage
Thrombosis
Transplant and Transplantation
Transplant rejection
Uterus, neoplasm
Vasodilation
Vasodilators
Viscosity
Vomiting
(liquid dosage compns. of **stable** nanoparticulate drugs)

IT Glycols, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)

IT Alditols
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)

IT Amine oxides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)

IT Amines, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)

IT Amino acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)

IT Biopolymers
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)

IT Carbohydrates, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)

IT Caseins, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)

IT Corticosteroids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)

IT Disaccharides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)

IT Fatty acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)

IT Flavonoids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)

IT Gelatins, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)

IT Glycerophospholipids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)
IT Minerals, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)
IT Monosaccharides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)
IT Peptides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)
IT Phosphates, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)
IT Phosphatidylserines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)
IT Phosphonium compounds
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)
IT Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)
IT Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)
IT Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)
IT Polysaccharides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)
IT Prostaglandins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)
IT Proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)
IT Quaternary ammonium compounds, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)
IT Safflower oil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)
IT Salts, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)
IT Sex hormones
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)
IT Sulfonium compounds
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)
IT Vitamins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)
IT Drug delivery systems
(liqs.; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Headache
(migraine; liquid dosage compns. of **stable** nanoparticulate drugs)

IT Drug delivery systems
(nanoparticles; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Drug delivery systems
(nasal; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Anti-inflammatory agents
(nonsteroidal; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Drug delivery systems
(ointments, creams; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Drug delivery systems
(ointments; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Drug delivery systems
(ophthalmic; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Contraceptives
Drug delivery systems
(oral; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Drug delivery systems
(parenterals; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Nerve, disease
(peripheral nerve injury; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Injury
(peripheral nerve; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Polyoxyalkylenes, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(phenolic; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phospholipid derivs.; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Nutrients
(plant; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Phenolic resins, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(polyoxyalkylene-; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Menopause
(postmenopause; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Intestinal bacteria
(probiotic; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Arthritis
(psoriatic arthritis; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Drug delivery systems
Infection
(pulmonary; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Drug delivery systems
(rectal; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(regulating agents; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Amines, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(salts; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Connective tissue, disease
(scleroderma; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Linum usitatissimum
(seeds; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Diet
(supplements; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Drug delivery systems
(suspensions, oral; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Lupus erythematosus
(systemic; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Drug delivery systems
(tablets; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Inflammation
(tendinitis; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Drug delivery systems
(topical; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Quaternary ammonium compounds, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tri-C8-10-alkylmethyl, chlorides; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Drug delivery systems
(vaginal; liquid dosage compns. of **stable** nanoparticulate drugs)
IT Adrenoceptor antagonists
(β-; liquid dosage compns. of **stable** nanoparticulate drugs)
IT 13598-36-2D, Phosphonic acid, alkylidenebis- derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Bisphosphonate; liquid dosage compns. of **stable** nanoparticulate drugs)
IT 7631-86-9, Silica, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(colloidal; liquid dosage compns. of **stable** nanoparticulate drugs)
IT 9004-06-2, Elastase 329900-75-6, COX-2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; liquid dosage compns. of **stable** nanoparticulate drugs)
IT 110-54-3, Hexane, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)
IT 50-35-1, Thalidomide 50-44-2, Mercaptopurine 50-53-3, Chlorpromazine, biological studies 50-78-2, Acetylsalicylic acid 50-99-7, Glucose, biological studies 52-53-9, Verapamil 56-81-5, Glycerol, biological studies 56-85-9, Glutamine, biological studies 57-09-0, Hexadecyltrimethylammonium bromide 57-11-4, Stearic acid, biological studies 57-48-7, Fructose, biological studies 57-50-1, Sucrose, biological studies 57-55-6, Propylene glycol, biological studies 57-88-5, Cholesterol, biological studies 58-32-2, Dipyridamole

59-30-3, Folic acid, biological studies 62-49-7D, Choline, esters 63-42-3, Lactose 64-17-5, Ethanol, biological studies 67-45-8, Furazolidone 69-65-8, Mannitol 69-89-6D, Xanthine, derivs. 73-31-4, Melatonin 75-65-0, biological studies 80-74-0, Acetylsulfisoxazole 87-99-0, Xylitol 99-20-7, Trehalose 102-71-6, Triethanolamine, biological studies 110-86-1D, Pyridine, quaternized, salts 112-00-5, Lauryltrimethylammonium chloride 123-03-5, CPC 129-03-3, Cyproheptadine 132-17-2, Benztropine mesylate 134-32-7D, 1-Naphthylamine, alkyldimethylammonium salts 139-07-1, Lauryldimethylbenzylammonium chloride 140-72-7, Cetylpyridinium bromide 143-67-9, Vinblastine sulfate 148-79-8, Thiabendazole 151-21-3, SDS, biological studies 154-42-7, Thioguanine 288-32-4D, Imidazole, quaternized, salts 303-53-7, Cyclobenzaprine 396-01-0, Triamterene 500-92-5, Proguanil 502-65-8, Lycopene 645-05-6, Altretamine 846-50-4, Temazepam 1119-94-4, Dodecyltrimethylammonium bromide 1119-97-7, Tetradecyltrimethylammonium bromide 1200-22-2, Lipoic acid 1327-43-1, Magnesium aluminum silicate 1592-23-0, Calcium Stearate 1643-19-2, Tetrabutylammonium bromide 1951-25-3, Amiodarone 1977-10-2, Loxapine 2062-78-4, Pimozide 2082-84-0, Decyltrimethylammonium bromide 2609-46-3, Amiloride 3416-24-8, Glucosamine 3458-28-4, Mannose 4205-90-7, Clonidine 4342-03-4, Dacarbazine 5137-55-3, Methyltrioctylammonium chloride 5350-41-4, Benzyltrimethylammonium bromide 7173-51-5, Dimethyldidecylammonium chloride 7281-04-1, Lauryldimethylbenzylammonium bromide 7447-40-7, Potassium chloride (KCl), biological studies 7647-14-5, Sodium chloride, biological studies 7786-30-3, Magnesium chloride (MgCl2), biological studies 9000-01-5, Gum acacia 9000-30-0D, Guar gum, cationic derivs. 9000-65-1, Tragacanth gum 9001-63-2, Lysozyme 9002-89-5, Poly(vinyl alcohol) 9003-39-8, Polyvinylpyrrolidone 9004-32-4 9004-34-6, Cellulose, biological studies 9004-54-0, Dextran, biological studies 9004-62-0, Hydroxyethyl cellulose 9004-64-2, Hydroxypropyl cellulose 9004-65-3, Hypromellose 9004-67-5, Methyl cellulose 9004-99-3, Polyethylene glycol stearate 9005-32-7, Alginic acid 9007-12-9, Calcitonin 9007-27-6, Chondroitin 9011-14-7, Poly(methyl methacrylate) 9011-14-7D, Poly(methyl methacrylate), hydrolyzed, trimethylammonium salts 9050-04-8, Cellulose, carboxymethyl ether, calcium salt 9050-31-1, Hydroxypropyl methyl cellulose phthalate 10118-90-8, Minocycline 12441-09-7D, Sorbitan, esters 13292-46-1, Rifampin 16679-58-6, Desmopressin 18186-71-5, Dodecyltriethylammonium bromide 24280-93-1 25086-89-9, Vinyl acetate-1-vinyl-2-pyrrolidone copolymer 25301-02-4, Ethylene oxide-formaldehyde-4-(1,1,3,3-Tetramethylbutyl)phenol copolymer 25322-68-3, Polyethylene glycol 25322-68-3D, Polyethylene glycol, phospholipid derivs. 26062-79-3, Poly(diallyldimethylammonium chloride) 27195-16-0, Sucrose distearate 27321-96-6, Polyethylene glycol cholesteryl ether 28228-56-0 28679-24-5, Dodecylbenzyltriethylammonium chloride 28981-97-7, Alprazolam 29094-61-9, Glipizide 29767-20-2, Teniposide 29836-26-8, n-Octyl-β-D-glucopyranoside 31431-39-7, Mebendazole 31566-31-1, Glyceryl monostearate 33419-42-0, Etoposide 34911-55-2, Bupropion 36735-22-5, Quazepam 37318-31-3, Sucrose stearate 38443-60-6, Decyltriethylammonium chloride 39809-25-1, Penciclovir 42399-41-7, Diltiazem 51264-14-3, Amsacrine 51569-39-2, Olin 10G 52128-35-5, Trimetrexate 52467-63-7, Tricetylmethylammonium chloride 55008-57-6 55268-75-2, Cefuroxime 55348-40-8, Triton X-200 58846-77-8, n-Decyl β-D-glucopyranoside 59080-45-4, n-Hexyl β-D-glucopyranoside 59122-55-3, n-DoDecyl β-D-glucopyranoside 59277-89-3, Acyclovir 65271-80-9, Mitoxantrone 65277-42-1, Ketoconazole 66085-59-4, Nimodipine 69227-93-6, n-DoDecyl β-D-maltoside 69984-73-2, n-Nonyl β-D-glucopyranoside 70458-96-7, Norfloxacin 72509-76-3, Felodipine 72558-82-8, Ceftazidime 72559-06-9, Rifabutin 73590-58-6, Omeprazole 76095-16-4, Enalapril maleate 76420-72-9, Enalaprilat 76824-35-6, Famotidine 78617-12-6, n-Heptyl β-D-glucopyranoside 79617-96-2, Sertraline 79794-75-5,

Loratadine 81098-60-4, Cisapride 81103-11-9, Clarithromycin 81409-90-7, Cabergoline 81859-24-7, Polyquat 10 82494-09-5, n-Decyl β-D-maltoside 84449-90-1, Raloxifene 85261-19-4, Nonanoyl-N-methylglucamide 85261-20-7, Decanoyl-N-methylglucamide 85316-98-9 85618-20-8, n-Heptyl β-D-thioglucopyranoside 85618-21-9, n-Octyl-β-D-thioglucopyranoside 85721-33-1, Ciprofloxacin 86386-73-4, Fluconazole 87679-37-6, Trandolapril 91161-71-6, Terbinafine 95233-18-4, Atovaquone 97322-87-7, Troglitazone 100286-97-3, Milrinone lactate 101397-87-9, D-Glucitol, 1-deoxy-1-[methyl(1-oxoheptyl)amino]- 103577-45-3, **Lansoprazole** 104987-11-3, Tacrolimus 106266-06-2, Risperidone 106392-12-5, Pluronic 107397-59-1, Tetronic 150R8 110617-70-4, Poloxamine 113665-84-2, Clopidogrel 115956-12-2, Dolasetron 127666-00-6 127779-20-8, Saquinavir 132539-06-1, Olanzapine 136817-59-9, Delavirdine 138402-11-6, Irbesartan 139481-59-7, Candesartan 139755-83-2, Sildenafil 144034-80-0, Rizatriptan 145599-86-6, Cerivastatin 147059-72-1, Trovafloxacin 159989-65-8, Nelfinavir mesylate 283158-20-3 329326-68-3, p-Isononylphenoxypolyglycidol 503178-50-5 608094-65-1, PEG-vitamin A 630400-66-7 630400-67-8 634601-99-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid dosage compns. of **stable** nanoparticulate drugs)

L2 ANSWER 11 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:41242 CAPLUS
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INVENTOR(S): Artalejo Ortega, Beatriz; Batllori Calbo, Javier; Fernandez Garcia, Andres; Julve Rubio, Jordi
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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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AB Disclosed are pharmaceutical formulations obtained by subjecting conventional microgranules to an external seal-coating layer that avoids the penetration of liquid vehicle, and selecting a hydrophobic liquid vehicle with a viscosity high enough not to wet the microgranules. The seal-coating layer may be obtained by coating the microgranules with an aqueous suspension comprising film formers and plasticizers. The liquid vehicle is comprised of oily solvents and viscosity agents. The formulation is presented in single dose sachets ready-to-use. This formulation enables the liquid oral administration of antiulcerous microgranules of

benzimidazoles, preferably **lansoprazole**, with several advantages comparing to com. available suspensions. The new formulation of **lansoprazole** microgranules has a similar bioavailability and slightly higher stability than conventional hard gelatin capsules. For example, conventional microgranules of **lansoprazole** were subjected to an addnl. seal coating with a composition containing hydroxypropyl Me cellulose 10, polyethylene glycol 5, and purified **water** q.s. to 100 %. The coated granules were suspended in an oily vehicle containing lauroyl macrogol-32 glyceride 4, ammonium glycyrrhizinate 0.5, Na saccharin 0.1, Na cyclamate 2, flavoring 1, and medium-chain glycerides balance to 100 %. The oily suspension obtained were packaged in single-dose sachets.

TI Long-term **stable** oral pharmaceutical formulation of microgranules in suspension

AB Disclosed are pharmaceutical formulations obtained by subjecting conventional microgranules to an external seal-coating layer that avoids the penetration of liquid vehicle, and selecting a hydrophobic liquid vehicle with a viscosity high enough not to wet the microgranules. The seal-coating layer may be obtained by coating the microgranules with an aqueous suspension comprising film formers and plasticizers. The liquid vehicle is comprised of oily solvents and viscosity agents. The formulation is presented in single dose sachets ready-to-use. This formulation enables the liquid oral administration of antiulcerous microgranules of benzimidazoles, preferably **lansoprazole**, with several advantages comparing to com. available suspensions. The new formulation of **lansoprazole** microgranules has a similar bioavailability and slightly higher stability than conventional hard gelatin capsules. For example, conventional microgranules of **lansoprazole** were subjected to an addnl. seal coating with a composition containing hydroxypropyl Me cellulose 10, polyethylene glycol 5, and purified **water** q.s. to 100 %. The coated granules were suspended in an oily vehicle containing lauroyl macrogol-32 glyceride 4, ammonium glycyrrhizinate 0.5, Na saccharin 0.1, Na cyclamate 2, flavoring 1, and medium-chain glycerides balance to 100 %. The oily suspension obtained were packaged in single-dose sachets.

ST antiulcer granule oral suspension bioavailability; **lansoprazole** granule cellulose ether coating suspension

IT Glycerides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medium-chain; seal-coated microgranules in liquid vehicles for manufacturing **stable** oral suspensions)

IT Antiulcer agents
Drug bioavailability
(seal-coated microgranules in liquid vehicles for manufacturing **stable** oral suspensions)

IT Corn oil
Lecithins
Peanut oil
Polyoxyalkylenes, biological studies
Soybean oil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(seal-coated microgranules in liquid vehicles for manufacturing **stable** oral suspensions)

IT Glycerides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(short-chain; seal-coated microgranules in liquid vehicles for manufacturing **stable** oral suspensions)

IT Drug delivery systems

(suspensions, oral; seal-coated microgranules in liquid vehicles for manufacturing **stable** oral suspensions)
IT 7631-86-9, Silica, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(colloidal; seal-coated microgranules in liquid vehicles for manufacturing **stable** oral suspensions)
IT 77-93-0, Triethyl citrate 88-99-3D, Phthalic acid, esters 109-43-3, Dibutyl decanedioate 112-92-5, Stearyl alcohol 9003-39-8, PVP 9004-65-3, Hydroxypropyl methyl cellulose 9005-32-7, Alginic acid 11138-66-2, Xanthan gum 24938-16-7, Eudragit EPO 25322-68-3, Polyethylene glycol 26942-95-0, Triisostearin 31566-31-1, Glyceryl monostearate 36653-82-4, Cetyl alcohol 103577-45-3, **Lansoprazole**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(seal-coated microgranules in liquid vehicles for manufacturing **stable** oral suspensions)

L2 ANSWER 12 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:242161 CAPLUS
DOCUMENT NUMBER: 138:260473
TITLE: Pharmaceutical formulations for protecting pharmaceutical compound from acidic environments
INVENTOR(S): Taneja, Rajneesh; Gupta, Pramrod
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024449	A1	20030327	WO 2002-US22229	20020712
W: CA, JP, MX				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR				
US 2003235628	A1	20031225	US 2001-955801	20010919
CA 2460987	AA	20030327	CA 2002-2460987	20020712
EP 1429766	A1	20040623	EP 2002-750005	20020712
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR, BG, CZ, EE, SK				
JP 2005507883	T2	20050324	JP 2003-528545	20020712
PRIORITY APPLN. INFO.:			US 2001-955801 A	20010919
			WO 2002-US22229 W	20020712

AB Pharmaceutical compns. for protecting acid-labile drugs, such as a proton pump inhibitor, in acidic environment comprise a protectant, i.e., a **water**-soluble or **water**-insol. acid neutralizer. For example, granules were prepared containing **lansoprazole** 30 mg, magnesium hydroxide 350 mg, calcium carbonate 140 mg, sucrose 120 mg, and tromethamine 350 mg. **Lansoprazole** was **stable** in the granules kept in a closed container at room temperature for 27 days.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB Pharmaceutical compns. for protecting acid-labile drugs, such as a proton pump inhibitor, in acidic environment comprise a protectant, i.e., a **water**-soluble or **water**-insol. acid neutralizer. For example, granules were prepared containing **lansoprazole** 30 mg, magnesium hydroxide 350 mg, calcium carbonate 140 mg, sucrose 120 mg, and tromethamine 350 mg. **Lansoprazole** was **stable** in the granules kept in a closed container at room temperature for 27 days.
IT 103577-45-3, **Lansoprazole**

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(acid neutralizers for protecting acid-labile drugs in acidic environment)

L2 ANSWER 13 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:173403 CAPLUS
DOCUMENT NUMBER: 138:210335
TITLE: **Stable** pharmaceutical compositions comprising acid labile benzimidazoles
INVENTOR(S): Sugaya, Masae; Shimizu, Toshihiro
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003017980	A1	20030306	WO 2002-JP8704	20020829
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2448760	AA	20030306	CA 2002-2448760	20020829
JP 2003327533	A2	20031119	JP 2002-251254	20020829
EP 1420763	A1	20040526	EP 2002-765367	20020829
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2004248939	A1	20041209	US 2004-487809	20040226

PRIORITY APPLN. INFO.:

JP 2001-263481	A	20010831
JP 2001-341477	A	20011107
JP 2002-60006	A	20020306
WO 2002-JP8704	W	20020829

OTHER SOURCE(S): MARPAT 138:210335

AB A solid composition, without enteric coating, contains an acid-labile active ingredient, particularly, a benzimidazole having an antiulcer activity. This composition neutralizes the acid in the stomach quickly, exerts quickly the pharmacol. effect of the drug and suppresses the formation of CO2. A gastric disintegrable solid composition contains in addition to the drug at least 1 component selected from metal oxides and metal hydroxides. The composition has a disintegration time of ≤7 min. **Lansoprazole** 240 g, 1160 g Mg(OH)2, 616 g D-mannitol, and 264 g corn starch were charged into a fluidized-bed granulator, and 8% aqueous solution prepared by dissolving 120 g of hydroxypropyl cellulose in 1380 g **water** was sprayed, and these materials were granulated, and dried to obtain 2188 g of granules (active ingredient group). Mg(OH)2 870 g, 1107 g of D-mannitol and 474 g of corn starch were charged in a fluidized bed granulator, and 750 g **water** was sprayed, and these materials were granulated, and dried to obtain 2199 g of granules (outer layer group). The active ingredient group 300 g, 408.5 g the outer layer group, 37.5 g Crospovidone and 11 g Mg stearate

were mixed in a bag to obtain a mixture The resultant mixture was compressed into tablets (750 mg/tablet). No darkishness by whittled powders or sticking of the mixture on the die was observed in the resulting tablets.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI **Stable** pharmaceutical compositions comprising acid labile benzimidazoles

AB A solid composition, without enteric coating, contains an acid-labile active ingredient, particularly, a benzimidazole having an antiulcer activity. This composition neutralizes the acid in the stomach quickly, exerts quickly the pharmacol. effect of the drug and suppresses the formation of CO2. A gastric disintegrable solid composition contains in addition to the drug at least 1 component selected from metal oxides and metal hydroxides. The composition has a disintegration time of ≤7 min. **Lansoprazole** 240 g, 1160 g Mg(OH)2, 616 g D-mannitol, and 264 g corn starch were charged into a fluidized-bed granulator, and 8% aqueous solution prepared by dissolving 120 g of hydroxypropyl cellulose in 1380 g **water** was sprayed, and these materials were granulated, and dried to obtain 2188 g of granules (active ingredient group). Mg(OH)2 870 g, 1107 g of D-mannitol and 474 g of corn starch were charged in a fluidized bed granulator, and 750 g **water** was sprayed, and these materials were granulated, and dried to obtain 2199 g of granules (outer layer group). The active ingredient group 300 g, 408.5 g the outer layer group, 37.5 g Crospovidone and 11 g Mg stearate were mixed in a bag to obtain a mixture The resultant mixture was compressed into tablets (750 mg/tablet). No darkishness by whittled powders or sticking of the mixture on the die was observed in the resulting tablets.

IT Carbonates, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkaline earth; **stable** pharmaceutical compns. comprising acid-labile benzimidazoles)

IT Drug delivery systems
(capsules; **stable** pharmaceutical compns. comprising acid-labile benzimidazoles)

IT Drug delivery systems
(granules; **stable** pharmaceutical compns. comprising acid-labile benzimidazoles)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proton pump, inhibitors; **stable** pharmaceutical compns. comprising acid-labile benzimidazoles)

IT Calcination
Surface area
(**stable** pharmaceutical compns. comprising acid-labile benzimidazoles)

IT Hydroxides (inorganic)
Oxides (inorganic), biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** pharmaceutical compns. comprising acid-labile benzimidazoles)

IT Drug delivery systems
(tablets; **stable** pharmaceutical compns. comprising acid-labile benzimidazoles)

IT 21645-51-2, Aluminum hydroxide (Al(OH)3), biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gels; **stable** pharmaceutical compns. comprising acid-labile benzimidazoles)

IT 1309-48-4, Magnesium oxide (MgO), biological studies
RL: FMU (Formation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)

(**stable** pharmaceutical compns. comprising acid-labile benzimidazoles)

IT 74-79-3, L-Arginine, biological studies 77-86-1, Trometamol 150-90-3, Disodium succinate 7558-79-4, DiSodium phosphate 7601-54-9, TriSodium phosphate
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** pharmaceutical compns. comprising acid-labile benzimidazoles)

IT 144-55-8, Carbonic acid monosodium salt, biological studies 471-34-1, Calcium carbonate, biological studies 546-93-0, Magnesium carbonate 1343-88-0, Magnesium silicate 12304-65-3, Hydrotalcite 12511-31-8 73590-58-6, Omeprazole 102625-70-7, Pantoprazole 103577-45-3, **Lansoprazole** 117976-89-3, Rabeprazole
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** pharmaceutical compns. comprising acid-labile benzimidazoles)

L2 ANSWER 14 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:958602 CAPLUS
DOCUMENT NUMBER: 138:29133
TITLE: Formulation of **stable** antiulcer oral preparations
INVENTOR(S): Machiba, Yasuo; Ikemoto, Keiichi; Tatsumi, Asaki; Asada, Kazuyoshi
PATENT ASSIGNEE(S): Towa Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002363080	A2	20021218	JP 2001-173557	20010608

PRIORITY APPLN. INFO.: JP 2001-173557 20010608

AB **Stable** antiulcer oral prepns., including enteric coated tablets, containing omeprazole, **lansoprazole**, and rabeprazole, and their alkali salts, are formulated by granulating and coating with film-forming **water**-soluble polymers and tableting with dispersing agents, etc.

TI Formulation of **stable** antiulcer oral preparations

AB **Stable** antiulcer oral prepns., including enteric coated tablets, containing omeprazole, **lansoprazole**, and rabeprazole, and their alkali salts, are formulated by granulating and coating with film-forming **water**-soluble polymers and tableting with dispersing agents, etc.

IT Antiulcer agents
Dispersing agents
Stability
(formulation of **stable** antiulcer oral prepns.)

IT Polymers, biological studies
Polyoxyalkylenes, biological studies
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(formulation of **stable** antiulcer oral prepns.)

IT Drug delivery systems
(oral; formulation of **stable** antiulcer oral prepns.)

IT Drug delivery systems
(tablets, enteric-coated; formulation of **stable** antiulcer oral prepns.)

IT 9004-64-2, Hydroxypropylcellulose 25322-68-3, PEG 6000 73590-58-6, Omeprazole 103577-45-3, **Lansoprazole** 117976-89-3,

Rabeprazole
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(formulation of **stable** antiulcer oral prepns.)

L2 ANSWER 15 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:636460 CAPLUS
DOCUMENT NUMBER: 137:159367
TITLE: Enteric coated preparations containing proton pump inhibitors
INVENTOR(S): Hirata, Kenji; Mori, Masaki
PATENT ASSIGNEE(S): Kyowa Yakuhin Kogyo K. K., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002234842	A2	20020823	JP 2001-77232	20010209
US 2004146558	A1	20040729	US 2003-352141	20030128

PRIORITY APPLN. INFO.: JP 2001-77232 A 20010209

AB This invention relates to **stable** enteric-soluble compns. which contain benzimidazole-type proton pump inhibitors. The compns. show little variation in drug release onset time. The compns. comprise (1) a core containing benzimidazoles as active ingredients and alkalies, (2) a **water**-insol. membrane coating containing dispersed **water** -soluble substance particles, and (3) an enteric-soluble coating. An enteric-coated tablet was formulated containing omeprazole 20, lactose 70, starch 21, low-substituted hydroxypropyl cellulose 6, hydroxypropyl cellulose 1, talc 2, and Mg stearate 1 mg.

AB This invention relates to **stable** enteric-soluble compns. which contain benzimidazole-type proton pump inhibitors. The compns. show little variation in drug release onset time. The compns. comprise (1) a core containing benzimidazoles as active ingredients and alkalies, (2) a **water**-insol. membrane coating containing dispersed **water** -soluble substance particles, and (3) an enteric-soluble coating. An enteric-coated tablet was formulated containing omeprazole 20, lactose 70, starch 21, low-substituted hydroxypropyl cellulose 6, hydroxypropyl cellulose 1, talc 2, and Mg stearate 1 mg.

IT 57-50-1, White sugar, biological studies 63-42-3, Lactose 69-65-8, D-Mannitol 99-20-7, Trehalose 144-55-8, Sodium hydrogen carbonate, biological studies 497-19-8, Sodium carbonate, biological studies 7632-05-5, Sodium phosphate 9004-38-0, Cellulose acetate phthalate 9004-57-3, Ethyl cellulose 9005-25-8, Starch, biological studies 9050-31-1, Hydroxypropyl methyl cellulose phthalate 25086-15-1, Methacrylic acidmethyl methacrylate copolymer 37205-99-5, Carboxymethyl ethyl cellulose 53237-50-6 71138-97-1, Hydroxypropyl methyl cellulose acetate succinate 73590-58-6, Omeprazole 102625-70-7, Pantoprazole 103577-45-3, **Lansoprazole** 117976-89-3, Rabeprazole
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enteric coated prepns. containing proton pump inhibitors)

L2 ANSWER 16 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:521408 CAPLUS
DOCUMENT NUMBER: 137:83661
TITLE: Pharmaceutical compositions containing a non-enteric coated proton pump inhibitor and a carbonate salt and bicarbonate salt combination
INVENTOR(S): Taneja, Rajneesh; Gupta, Pramod

PATENT ASSIGNEE(S): Tap Pharmaceutical Products, Inc., USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053097	A2	20020711	WO 2001-US48320	20011212
WO 2002053097	A3	20030130		
W: CA, JP, MX				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2432184	AA	20020711	CA 2001-2432184	20011212
EP 1353624	A2	20031022	EP 2001-991084	20011212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
JP 2004525100	T2	20040819	JP 2002-554048	20011212
PRIORITY APPLN. INFO.:			US 2000-750430 A	20001228
			WO 2001-US48320 W	20011212

AB A method for treating gastric acid disorders with a non-enteric coated proton pump inhibitor in a carrier including a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal; and a pharmaceutical composition of a non-enteric coated proton pump inhibitor in a carrier including a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal are disclosed. A preferred proton pump inhibitor is **lansoprazole**, a preferred bicarbonate salt is sodium bicarbonate, and a preferred carbonate salt is sodium carbonate. The composition is a fast-acting formulation which reduces the undesirable belching associated with proton pump inhibitor formulations that contain high doses of sodium bicarbonate. Granular formulations of **lansoprazole** for this example were prepared as follows. Sucrose (60 g) was dissolved in **water** with gentle heating to form a 60% solution Then, 46.93 g Na2CO3 and 37.17 g NaHCO3 were mixed together thoroughly. Subsequently, 35 g this mixture (carbicarb), 7.5 g lactose and 1.5 g **lansoprazole** were transferred to a mortar and mixed vigorously. The 60% sucrose solution (6 mL) was gradually added to the mortar while mixing with a pestle to form a coherent, wetted mass. This coherent mass was passed through a 10-mesh screen and the resulting granules were dried at 50° for 12 h. **Lansoprazole**, when formulated with carbicarb as granules, was **stable** in simulated gastric fluid for at least 60 min.
AB A method for treating gastric acid disorders with a non-enteric coated proton pump inhibitor in a carrier including a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal; and a pharmaceutical composition of a non-enteric coated proton pump inhibitor in a carrier including a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal are disclosed. A preferred proton pump inhibitor is **lansoprazole**, a preferred bicarbonate salt is sodium bicarbonate, and a preferred carbonate salt is sodium carbonate. The composition is a fast-acting formulation which reduces the undesirable belching associated with proton pump inhibitor formulations that contain high doses of sodium bicarbonate. Granular formulations of **lansoprazole** for this example were prepared as follows. Sucrose (60 g) was dissolved in **water** with gentle heating to form a 60% solution Then, 46.93 g Na2CO3 and 37.17 g NaHCO3 were mixed together thoroughly. Subsequently, 35 g this mixture (carbicarb), 7.5 g lactose and 1.5 g **lansoprazole** were transferred to a mortar and mixed vigorously. The 60% sucrose solution (6 mL) was gradually added to the mortar while mixing with a pestle to form a coherent, wetted mass. This coherent mass was passed through a 10-mesh screen and the resulting granules were dried at 50° for 12

h. **Lansoprazole**, when formulated with carbicarb as granules, was **stable** in simulated gastric fluid for at least 60 min.

IT 103577-45-3, **Lansoprazole**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceuticals containing non-enteric coated proton pump inhibitors and carbonate salt and bicarbonate salt combination)

L2 ANSWER 17 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:185616 CAPLUS
DOCUMENT NUMBER: 136:252482
TITLE: Preparation of aqueous clear solution dosage forms with bile acids
INVENTOR(S): Yoo, Seo Hong
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 35 pp., Cont.-in-part of U. S. 6,251,428.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2002031558	A1	20020314	US 2001-778154		20010205
US 6251428	B1	20010626	US 1999-357549		19990720
US 2003186933	A1	20031002	US 2002-309603		20021204
PRIORITY APPLN. INFO.:			US 1998-94069P	P	19980724
			US 1999-357549	A2	19990720
			US 2000-180268P	P	20000204
			US 2001-778154	A3	20010205

AB Compns. for pharmaceutical and other uses comprise clear aqueous solns. of bile acids which do not form any detectable ppts. over selected ranges of pH values of the aqueous solution The compns. comprise (i) **water**, (ii) a bile acid component in the form of a bile acid, bile acid salt, or a bile acid conjugated with an amine by an amide linkage; and (iii) either or both an aqueous soluble starch conversion product and an aqueous soluble non-starch polysaccharide. The composition remains in solution without forming a precipitate over a range of pH values and, according to one embodiment, remains in solution for all pH values obtainable in an aqueous system. The composition may further contain a pharmaceutical compound, such as insulin, heparin, bismuth compds., amantadine and rimantadine. For example, solution dosage forms that did not show any precipitation at any pH were prepared containing ursodeoxycholic acid (UDCA) 22 g, 1N NaOH 75 mL, chenodeoxycholic acid (CDCA) 3 g, maltodextrin 875 g, bismuth citrate 4 g, citric acid or lactic acid as needed, and purified **water** to make 1 L.

AB Compns. for pharmaceutical and other uses comprise clear aqueous solns. of bile acids which do not form any detectable ppts. over selected ranges of pH values of the aqueous solution The compns. comprise (i) **water**, (ii) a bile acid component in the form of a bile acid, bile acid salt, or a bile acid conjugated with an amine by an amide linkage; and (iii) either or both an aqueous soluble starch conversion product and an aqueous soluble non-starch polysaccharide. The composition remains in solution without forming a precipitate over a range of pH values and, according to one embodiment, remains in solution for all pH values obtainable in an aqueous system. The composition may further contain

a pharmaceutical compound, such as insulin, heparin, bismuth compds., amantadine and rimantadine. For example, solution dosage forms that did not show any precipitation at any pH were prepared containing ursodeoxycholic acid (UDCA) 22 g, 1N NaOH 75 mL, chenodeoxycholic acid (CDCA) 3 g, maltodextrin 875 g, bismuth citrate 4 g, citric acid or lactic acid as needed, and purified **water** to make 1 L.

IT Antihistamines
(H2; preparation of **stable** aqueous solns. containing bile acids for therapy)

IT Bile acids
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(O-sulfonated derivs.; preparation of **stable** aqueous solns. containing bile acids for therapy)

IT Amines, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(aliphatic; preparation of **stable** aqueous solns. containing bile acids for therapy)

IT Carbohydrates, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(amino sugars; preparation of **stable** aqueous solns. containing bile acids for therapy)

IT Glycosides
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bile acid; preparation of **stable** aqueous solns. containing bile acids for therapy)

IT Avena sativa
Zea mays
(bran; preparation of **stable** aqueous solns. containing bile acids for therapy)

IT Amino acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(branched; preparation of **stable** aqueous solns. containing bile acids for therapy)

IT Antitumor agents
Intestine, neoplasm
(colorectal adenoma; preparation of **stable** aqueous solns. containing bile acids for therapy)

IT Adenoma
(colorectal; preparation of **stable** aqueous solns. containing bile acids for therapy)

IT Bile acids
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates, with amines; preparation of **stable** aqueous solns. containing bile acids for therapy)

IT Amines, biological studies
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates, with bile acids; preparation of **stable** aqueous solns. containing bile acids for therapy)

IT Bran
(corn; preparation of **stable** aqueous solns. containing bile acids for therapy)

IT Bath preparations
(douches; preparation of **stable** aqueous solns. containing bile acids for therapy)

IT Acacia
(emulsifying agent; preparation of **stable** aqueous solns. containing bile

acids for therapy)
IT Drug delivery systems
(enemas; preparation of **stable** aqueous solns. containing bile acids for therapy)
IT Glycyrrhiza
(exts.; preparation of **stable** aqueous solns. containing bile acids for therapy)
IT Micelles
(forming materials; preparation of **stable** aqueous solns. containing bile acids for therapy)
IT Inflammation
Stomach, disease
(gastritis; preparation of **stable** aqueous solns. containing bile acids for therapy)
IT Bile acids
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glycosides; preparation of **stable** aqueous solns. containing bile acids for therapy)
IT Amines, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(heterocyclic; preparation of **stable** aqueous solns. containing bile acids for therapy)
IT Syrups (sweetening agents)
(hydrolyzed starch; preparation of **stable** aqueous solns. containing bile acids for therapy)
IT Drug delivery systems
(injections; preparation of **stable** aqueous solns. containing bile acids for therapy)
IT Drug delivery systems
(liqs., oral; preparation of **stable** aqueous solns. containing bile acids for therapy)
IT Drug delivery systems
(nasal; preparation of **stable** aqueous solns. containing bile acids for therapy)
IT Bran
(oat; preparation of **stable** aqueous solns. containing bile acids for therapy)
IT Drug delivery systems
(otic; preparation of **stable** aqueous solns. containing bile acids for therapy)
IT Drug delivery systems
(pastes; preparation of **stable** aqueous solns. containing bile acids for therapy)
IT Ulcer
(peptic; preparation of **stable** aqueous solns. containing bile acids for therapy)
IT Albizia lebbek
Andrographis paniculata
Antibiotics
Antiulcer agents
Azadirachta indica
Calculi, biliary
Cosmetics
Curcuma longa
Dietary fiber
Emulsifying agents
Gymnema sylvestre
Helicobacter pylori
Human
Hypolipemic agents
Justicia adhatoda

Liver, disease
Momordica charantia
Moringa pterygosperma
Mouthwashes
Picrorhiza kurrooa
Protozoacides
Skin preparations (pharmaceutical)
Stability
Terminalia arjuna
Tinospora cordifolia
Wheat bran
(preparation of **stable** aqueous solns. containing bile acids for therapy)

IT Bile acids
Bile salts
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of **stable** aqueous solns. containing bile acids for therapy)

IT Amino acids, biological studies
Interferons
Vitamins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of **stable** aqueous solns. containing bile acids for therapy)

IT Bases, reactions
Quaternary ammonium compounds, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of **stable** aqueous solns. containing bile acids for therapy)

IT Polysaccharides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of **stable** aqueous solns. containing bile acids for therapy)

IT Drug delivery systems
(solns.; preparation of **stable** aqueous solns. containing bile acids for therapy)

IT Drug delivery systems
(syrups; preparation of **stable** aqueous solns. containing bile acids for therapy)

IT Drug delivery systems
(topical; preparation of **stable** aqueous solns. containing bile acids for therapy)

IT Digestive tract, disease
(ulcer, peptic; preparation of **stable** aqueous solns. containing bile acids for therapy)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α; preparation of **stable** aqueous solns. containing bile acids for therapy)

IT 9000-07-1, Carrageenan 9000-30-0, Guar gum 9000-65-1, Tragacanth gum 9000-69-5, Pectin 9002-89-5, Polyvinyl alcohol 9003-39-8, Povidone 9004-32-4, Carboxymethyl cellulose sodium 9004-64-2, Hydroxypropyl cellulose 9004-67-5, Methyl cellulose 11138-66-2, Xanthan gum 12441-09-7D, Sorbitan, esters 37353-59-6, Hydroxymethyl cellulose
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emulsifying agent; preparation of **stable** aqueous solns. containing bile acids for therapy)

IT 8063-16-9, Psyllium
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fiber; preparation of **stable** aqueous solns. containing bile acids for therapy)

IT 9004-34-6, Cellulose, biological studies 73020-09-4, Oat gum

393123-34-7, Soybean gum
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of **stable** aqueous solns. containing bile acids for therapy)

IT 81-25-4, Cholic acid 83-44-3, Deoxycholic acid 83-44-3D, Deoxycholic acid, Iodonated 83-49-8, Hyodeoxycholic acid 128-13-2, Ursodeoxycholic acid 434-13-9, Lithocholic acid 474-25-9, Chenodeoxycholic acid 516-35-8, Taurochenodeoxycholic acid 516-50-7, Taurodeoxycholic acid 547-75-1, Iocholic acid 640-79-9, Glycochenodeoxycholic acid 4651-67-6, 7-Ketolithocholic acid 12619-70-4D, Cyclodextrin, complexes with bile acids 14605-22-2, Tauroursodeoxycholic acid 64480-66-6, Glycoursodeoxycholic acid
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of **stable** aqueous solns. containing bile acids for therapy)

IT 112-24-3, Trientine
RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(preparation of **stable** aqueous solns. containing bile acids for therapy)

IT 50-02-2, Dexamethasone 50-03-3 50-23-7, Hydrocortisone 50-24-8, Prednisolone 50-44-2, Mercaptopurine 50-60-2, Phentolamine 50-78-2, Acetylsalicylic acid 51-21-8, Fluorouracil 52-28-8, Codeine phosphate 52-53-9, Verapamil 52-67-5, D-Penicillamine 53-03-2, Prednisone 53-06-5, Cortisone 53-86-1, Indomethacin 54-05-7, Chloroquine 54-42-2, Idoxuridine 55-63-0, Nitroglycerin 56-81-5, Glycerin, biological studies 57-96-5, Sulfinpyrazone 58-00-4, Apomorphine 58-32-2, Dipyridamole 58-55-9, Theophylline, biological studies 59-05-2, Methotrexate 59-67-6, Niacin, biological studies 60-54-8, Tetracycline 61-68-7, Mefenamic acid 61-90-5, L-Leucine, biological studies 63-89-8, Colfosceril palmitate 64-31-3, Morphine sulfate 64-73-3, Demeclocycline hydrochloride 64-77-7, Tolbutamide 64-86-8, Colchicine 67-96-9, Dihydrotachysterol 69-53-4, Ampicillin 70-00-8, Trifluridine 72-18-4, L-Valine, biological studies 73-32-5, L-Isoleucine, biological studies 76-25-5, Triamcinolone acetonide 76-57-3, Codeine 78-11-5, Pentaerythrityl tetranitrate 79-57-2, Oxytetracycline 83-43-2, Methyl prednisolone 87-33-2, Isosorbide dinitrate 89-57-6, Mesalamine 93-14-1, Guaifenesin 94-20-2, Chlorpropamide 107-35-7, Taurine 114-07-8, Erythromycin 118-42-3, Hydroxychloroquine 124-94-7, Triamcinolone 125-69-9, Dextromethorphan hydrobromide 126-07-8, Griseofulvin 140-64-7, Pentamidine isethionate 143-71-5, Hydrocodone bitartrate 146-48-5, Yohimbin 147-24-0, Diphenhydramine hydrochloride 154-23-4, Catechin (flavan) 299-42-3, Ephedrine 304-20-1, Hydralazine hydrochloride 305-03-3, Chlorambucil 315-30-0, Allopurinol 317-34-0, Aminophylline 320-67-2, Azacitidine 364-98-7, Diazoxide 378-44-9, Betamethasone 443-48-1, Metronidazole 446-86-6, Azathioprine 479-18-5, Dyphylline 506-87-6, Ammonium carbonate 514-36-3, Fludrocortisone acetate 530-08-5, Isoetharine 536-24-3, Ethylnorepinephrine 564-25-0, Doxycycline 579-56-6, Isoxsuprine hydrochloride 586-06-1, Metaproterenol 616-91-1, Acetylcysteine 665-66-7, Amantadine hydrochloride 745-65-3, Alprostadil 768-94-5, Amantadine 777-11-7, Haloprogin 849-55-8, Nylidrin hydrochloride 1095-90-5, Methadone hydrochloride 1115-70-4, Metformin hydrochloride 1397-89-3, Amphotericin B 1400-61-9, Nystatin 1405-86-3, Glycyrrhizin 1420-53-7, Codeine sulfate 1501-84-4, Rimantadine hydrochloride 1951-25-3, Amiodarone 2451-01-6, Terpin hydrate 3056-17-5, Stavudine 3385-03-3, Flunisolide 4205-91-8, Clonidine hydrochloride 4428-95-9, Foscarnet 5178-19-8 5534-09-8, Beclomethasone dipropionate 6591-52-2 7232-21-5, Metoclopramide hydrochloride 7440-69-9D, Bismuth, compds. 7481-89-2, Zalcitabine 7683-59-2, Isoproterenol 9004-10-8, Insulin, biological studies 9005-49-6, Heparin, biological studies 9007-12-9, Calcitonin 9007-92-5, Glucagon, biological studies 9035-68-1, Proinsulin

10238-21-8, Glyburide 12125-02-9, Ammonium chloride, biological studies 12192-57-3, Aurothioglucose 12244-57-4, Gold sodium thiomalate 13392-18-2, Fenoterol 13392-28-4, Rimantadine 13614-98-7, Minocycline hydrochloride 14769-73-4, Levamisole 15000-04-1 15687-27-1, Ibuprofen 15826-37-6, Cromolyn sodium 18559-94-9, Albuterol 19237-84-4, Prazosin hydrochloride 19794-93-5, Trazodone 21829-25-4, Nifedipine 22204-53-1, Naproxen 22254-24-6, Ipratropium bromide 22494-42-4, Diflunisal 22916-47-8, Miconazole 23031-32-5, Terbutaline sulfate 23593-75-1, Clotrimazole 24169-02-6, Econazole nitrate 25717-80-0, Molsidomine 26787-78-0, Amoxicillin 28300-74-5, Antimony potassium tartrate 29094-61-9, Glipizide 30392-40-6, Bitolterol 30516-87-1, Zidovudine 31586-77-3, Bismuth sodium tartrate 32222-06-3, Calcitriol 34031-32-8, Auranofin 35711-34-3, Tolmetin sodium 36322-90-4, Piroxicam 36703-88-5, Isoprinosine 36791-04-5, Ribavirin 38260-01-4, Trientine hydrochloride 38304-91-5, Minoxidil 38677-81-5, Pirbuterol 39809-25-1, Penciclovir 42399-41-7, Diltiazem 50370-12-2, Cefadroxil 51110-01-1, Somatostatin 51333-22-3, Budesonide 51481-61-9, Cimetidine 53678-77-6, Muramyl dipeptide 53994-73-3, Cefaclor 54182-58-0, Sucralfate 56180-94-0, Acarbose 59122-46-2, Misoprostol 59277-89-3, Acyclovir 61318-91-0, Sulconazole nitrate 63074-08-8, Terazosin hydrochloride 63585-09-1, Foscarnet sodium 63675-72-9, Nisoldipine 64211-46-7, Oxiconazole nitrate 64706-54-3, Bepridil 65277-42-1, Ketoconazole 66357-35-5, Ranitidine 66357-59-3, Ranitidine hydrochloride 69655-05-6, Didanosine 73590-58-6, Omeprazole 75330-75-5, Lovastatin 75695-93-1, Isradipine 76824-35-6, Famotidine 76963-41-2, Nizatidine 77883-43-3, Doxazosin mesylate 78628-80-5, Terbinafine hydrochloride 79902-63-9, Simvastatin 80474-14-2, Fluticasone propionate 81103-11-9, Clarithromycin 81131-70-6, Pravastatin sodium 83150-76-9, Octreotide 83881-52-1, Cetirizine dihydrochloride 83905-01-5, Azithromycin 84625-61-6, Itraconazole 86386-73-4, Fluconazole 89365-50-4, Salmeterol 91980-85-7 93957-55-2, Fluvastatin sodium 95233-18-4, Atovaquone 103577-45-3, **Lansoprazole** 104227-87-4, Famciclovir 107753-78-6, Zafirlukast 107910-75-8, Ganciclovir sodium 111406-87-2, Zileuton 113852-37-2, Cidofovir 124832-27-5, Valacyclovir hydrochloride 129618-40-2, Nevirapine 133107-64-9, Insulin lispro 134523-03-8, Atorvastatin-calcium 134678-17-4, Lamivudine 135062-02-1, Repaglinide 139755-83-2, Sildenafil 143201-11-0, Cerivastatin sodium 147221-93-0, Delavirdine mesylate 149845-06-7, Saquinavir mesylate 151767-02-1, Montelukast sodium 155213-67-5, Ritonavir 157810-81-6, Indinavir sulfate 159989-65-8, Nelfinavir mesylate 171599-83-0, Sildenafil citrate 403804-21-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of **stable** aqueous solns. containing bile acids for therapy)

IT 50-21-5, Lactic acid, reactions 56-87-1, L-Lysine, reactions 60-00-4, Edetic acid, reactions 62-49-7, Choline 70-26-8, L-Ornithine 74-79-3, L-Arginine, reactions 77-92-9, Citric acid, reactions 87-69-4, Tartaric acid, reactions 102-71-6, Triethanolamine, reactions 110-85-0, Piperazine, reactions 110-85-0D, Piperazine, N-alkyl derivs. 110-89-4, Piperidine, reactions 110-89-4D, Piperidine, N-alkyl derivs. 110-91-8, Morpholine, reactions 110-91-8D, Morpholine, N-alkyl derivs. 111-40-0, Diethylene triamine 112-57-2, Tetraethylene pentamine 123-75-1, Pyrrolidine, reactions 488-43-7, D-Glucamine 6915-15-7, Malic acid 7664-41-7, Ammonia, reactions 14002-32-5, Trimethanolamine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of **stable** aqueous solns. containing bile acids for therapy)

IT 50-99-7, D-Glucose, biological studies 9004-53-9, Dextrin 9004-54-0, Dextran, biological studies 9005-25-8, Starch, biological studies 9050-36-6, Maltodextrin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of **stable** aqueous solns. containing bile acids for therapy)

L2 ANSWER 18 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:635890 CAPLUS
DOCUMENT NUMBER: 135:185502
TITLE: Orally administrable acid-**stable** antiulcer benzimidazole polymeric derivatives
INVENTOR(S): Mali, Subhash; Gupte, Rajan; Deshpande, Jayant; Ranbhan, Kamlesh
PATENT ASSIGNEE(S): Kopran Research Laboratories Limited, India
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001062248	A1	20010830	WO 2000-IN16	20000224
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2400953	AA	20010830	CA 2000-2400953	20000224
EP 1257269	A1	20021120	EP 2000-939036	20000224
EP 1257269	B1	20041103		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003523386	T2	20030805	JP 2001-561314	20000224
BR 2000017140	A	20040525	BR 2000-17140	20000224
AT 281164	E	20041115	AT 2000-939036	20000224
US 2002038032	A1	20020328	US 2001-964442	20010928
US 2003023091	A9	20030130		
US 6617338	B2	20030909		
ZA 2002006649	A	20030820	ZA 2002-6649	20020820

PRIORITY APPLN. INFO.: WO 2000-IN16 W 20000224
OTHER SOURCE(S): MARPAT 135:185502
AB Orally administrable acid **stable** anti-ulcer benzimidazole derivs. which are polymer based, are prepared The process of preparation comprises condensing a benzimidazole with a biocompatible partially orally biodegradable synthetic crosslinked polymer in aqueous medium at 5-80° and pH 4-11 under an inert atmospheric The percent weight of benzimidazole with respect to the polymeric conjugate is 1-50. The reaction mixture is cooled and the product is isolated and dried at 25-45°. There is also provided a formulation of the polymeric benzimidazoles in combination with excipients. Thus, a copolymer from acrylamide and glycidyl methacrylate was allowed to react with omeprazole to give a polymer-substituted drug. Tablet contained the above polymer-substituted omeprazole 100.0, lactose 70.0, Mg stearate 1.5, Me cellulose 0.6, and crospovidone 5.5 g, and **water** qs.
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Orally administrable acid-**stable** antiulcer benzimidazole polymeric derivatives
AB Orally administrable acid **stable** anti-ulcer benzimidazole derivs. which are polymer based, are prepared The process of preparation

comprises condensing a benzimidazole with a biocompatible partially orally biodegradable synthetic crosslinked polymer in aqueous medium at 5-80° and pH 4-11 under an inert atmospheric The percent weight of benzimidazole with respect to the polymeric conjugate is 1-50. The reaction mixture is cooled and the product is isolated and dried at 25-45°. There is also provided a formulation of the polymeric benzimidazoles in combination with excipients. Thus, a copolymer from acrylamide and glycidyl methacrylate was allowed to react with omeprazole to give a polymer-substituted drug. Tablet contained the above polymer-substituted omeprazole 100.0, lactose 70.0, Mg stearate 1.5, Me cellulose 0.6, and crospovidone 5.5 g, and **water** qs.

IT Drug delivery systems
(capsules; orally administrable acid-**stable** antiulcer benzimidazole polymeric derivs.)

IT Antiulcer agents
(orally administrable acid-**stable** antiulcer benzimidazole polymeric derivs.)

IT Drug delivery systems
(suspensions; orally administrable acid-**stable** antiulcer benzimidazole polymeric derivs.)

IT Drug delivery systems
(tablets; orally administrable acid-**stable** antiulcer benzimidazole polymeric derivs.)

IT 51-17-2DP, benzimidazole, derivs. 31743-77-8DP, Ethylene glycol dimethacrylate-glycidyl methacrylate copolymer, reaction products with imidazoles 55031-95-3DP, Acrylamide-glycidyl methacrylate copolymer, reaction products with imidazoles 73590-58-6DP, Omeprazole, reaction products with polymers 85075-35-0DP, Acrylonitrile-ethylene glycol dimethacrylate-glycidyl acrylate copolymer, reaction products with imidazoles 102625-70-7DP, Pantoprazole, reaction products with polymers 103577-45-3DP, **Lansoprazole**, reaction products with polymers
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(orally administrable acid-**stable** antiulcer benzimidazole polymeric derivs.)

L2 ANSWER 19 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:450876 CAPLUS
DOCUMENT NUMBER: 135:51076
TITLE: New **stable** multi-unitary pharmaceutical preparations containing substituted benzimidazoles
INVENTOR(S): Goncalves Mendes, Carla Patricia; Caeiro Ramalho De Oliveira, Maria Julia
PATENT ASSIGNEE(S): Laboratorio Medinfar-Produtos Farmaceuticos, S.A., Port.
SOURCE: Eur. Pat. Appl., 28 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1108425	A1	20010620	EP 1999-670010	19991216
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6379705	B1	20020430	US 2000-580551	20000530

PRIORITY APPLN. INFO.: EP 1999-670010 A 19991216

AB The present invention relates to new oral multi-unitary pharmaceutical

prepns. containing substituted benzimidazoles as inhibitors of H+,K+-ATPase (i.e., omeprazole, **lansoprazole**, pantoprazole, leminoprazole and pariprazole) or their pharmaceutically acceptable salts. Such pharmaceutical prepns. are **stable** pellet prepns. containing substituted benzimidazole(s) or their salts and they comprise a quantity of active ingredient of 1-50 mg, an inert core of spherical symmetry with a diameter of 600-1000 μm, constituted by inert excipients, coated with an active layer containing at least one substituted benzimidazole in the micronized form and various pharmaceutically acceptable inert excipients, mixed in suitable proportions in order to allow the disaggregation of the formulations and dissoln. of the active ingredient(s) in an appropriate manner, coated in turn with an insulating layer of a polymer soluble in **water**, free from alkaline and/or alkaline-earthy metallic salts, of a min. thickness of 15 μm, this layer being coated lastly with a gastro-resistant or enteric layer of a min. thickness of 30 μm. This invention also refers to the process for the preparation of said pharmaceutical prepns.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI New **stable** multi-unitary pharmaceutical preparations containing substituted benzimidazoles

AB The present invention relates to new oral multi-unitary pharmaceutical prepns. containing substituted benzimidazoles as inhibitors of H+,K+-ATPase (i.e., omeprazole, **lansoprazole**, pantoprazole, leminoprazole and pariprazole) or their pharmaceutically acceptable salts. Such pharmaceutical prepns. are **stable** pellet prepns. containing substituted benzimidazole(s) or their salts and they comprise a quantity of active ingredient of 1-50 mg, an inert core of spherical symmetry with a diameter of 600-1000 μm, constituted by inert excipients, coated with an active layer containing at least one substituted benzimidazole in the micronized form and various pharmaceutically acceptable inert excipients, mixed in suitable proportions in order to allow the disaggregation of the formulations and dissoln. of the active ingredient(s) in an appropriate manner, coated in turn with an insulating layer of a polymer soluble in **water**, free from alkaline and/or alkaline-earthy metallic salts, of a min. thickness of 15 μm, this layer being coated lastly with a gastro-resistant or enteric layer of a min. thickness of 30 μm. This invention also refers to the process for the preparation of said pharmaceutical prepns.

IT 73590-58-6, Omeprazole 102625-70-7, Pantoprazole 103577-45-3, **Lansoprazole** 104340-86-5, Leminoprazole 117976-89-3, Pariprazole
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of multi-unitary enteric-coated pellet prepns. containing substituted benzimidazoles)

L2 ANSWER 20 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:475425 CAPLUS
DOCUMENT NUMBER: 133:94537
TITLE: Pharmaceutical formulations containing inclusion amino acid salts compounds of benzimidazole derivatives with cyclodextrins
INVENTOR(S): Mendes Cerdeira, Ana Maria; De Sousa Goucha, Jorge Pedro Manuel
PATENT ASSIGNEE(S): Tecnimede-Sociedade Tecnico-Medicinal, S.A., Port.
SOURCE: Eur. Pat. Appl., 27 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1018340	A1	20000712	EP 1999-670003	19990106
EP 1018340	B1	20030910		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 249218	E	20030915	AT 1999-670003	19990106
PT 1018340	T	20031231	PT 1999-670003	19990106
ES 2149750	T3	20040601	ES 1999-670003	19990106
PRIORITY APPLN. INFO.:			EP 1999-670003 A	19990106

AB The present invention concerns new very **stable** inclusion compds. from a hydrosol. basic amino acid salt of a benzimidazole derivative, namely omeprazole, **lansoprazole** and pantoprazole, and one or more cyclodextrins, preferably β-cyclodextrin; the process of their preparation, and their use in the manufacture of a medicine for the prophylactic and therapeutic treatment of duodenal gastric ulcer, gastro esophageal reflow disease and Zollinger-Ellison-syndrome are also disclosed. To a solution of 7.4 g L-arginine in 200 mL of **water** was added 3.0 g omeprazole followed by addition of 2.68 g of β-cyclodextrin and stirred for 2 h. After the lyophilization, the resulting inclusion compound (1:5:2) was kept at 40° and 75% RH for 6 mo to show degradation products of 0.8%. A tablet contained the above inclusion compound 86.8, microcryst. cellulose 213.0, colloidal silica 3.0, and magnesium stearate 3.0 g.

AB The present invention concerns new very **stable** inclusion compds. from a hydrosol. basic amino acid salt of a benzimidazole derivative, namely omeprazole, **lansoprazole** and pantoprazole, and one or more cyclodextrins, preferably β-cyclodextrin; the process of their preparation, and their use in the manufacture of a medicine for the prophylactic and therapeutic treatment of duodenal gastric ulcer, gastro esophageal reflow disease and Zollinger-Ellison-syndrome are also disclosed. To a solution of 7.4 g L-arginine in 200 mL of **water** was added 3.0 g omeprazole followed by addition of 2.68 g of β-cyclodextrin and stirred for 2 h. After the lyophilization, the resulting inclusion compound (1:5:2) was kept at 40° and 75% RH for 6 mo to show degradation products of 0.8%. A tablet contained the above inclusion compound 86.8, microcryst. cellulose 213.0, colloidal silica 3.0, and magnesium stearate 3.0 g.

L2 ANSWER 21 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:639980 CAPLUS
DOCUMENT NUMBER: 131:341883
TITLE: Effect of various salts on the stability of **lansoprazole**, omeprazole, and pantoprazole as determined by high-performance liquid chromatography
AUTHOR(S): Ekpe, Anthony; Jacobsen, Thomas
CORPORATE SOURCE: Bayer Corporation, Morristown, NJ, 07962-1910, USA
SOURCE: Drug Development and Industrial Pharmacy (1999), 25(9), 1057-1065
CODEN: DDIPD8; ISSN: 0363-9045
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A fast and reproducible reversed-phase HPLC method was developed for the simultaneous determination of omeprazole, **lansoprazole**, and pantoprazole. The 3 compds. were monitored at 280 nm by using Zorbax Eclipse XDB C8 (5 μm, 150 cm + 4.6 mm i.d.) and a mobile phase consisting of 700:300 phosphate buffer-MeCN with the pH adjusted to 7.0 with phosphoric acid. The method was used to study the effect of pH and various salts on the stability of the 3 compds. The pH rate profile curve

showed that pantoprazole was the most **stable** compound and **lansoprazole** the least **stable**. The stabilities of the compds. in salt solns. were in the following order: phosphate buffer < trisodium citrate < citrate buffer ≤ acetate buffer < citric acid ≤ monosodium citrate ≤ calcium carbonate < sodium bicarbonate < sodium chloride < **water**. The rate of degradation had a direct relationship with the H+ and salt concentration

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Effect of various salts on the stability of **lansoprazole**, omeprazole, and pantoprazole as determined by high-performance liquid chromatography

AB A fast and reproducible reversed-phase HPLC method was developed for the simultaneous determination of omeprazole, **lansoprazole**, and pantoprazole. The 3 compds. were monitored at 280 nm by using Zorbax Eclipse XDB C8 (5 μm, 150 cm + 4.6 mm i.d.) and a mobile phase consisting of 700:300 phosphate buffer-MeCN with the pH adjusted to 7.0 with phosphoric acid. The method was used to study the effect of pH and various salts on the stability of the 3 compds. The pH rate profile curve showed that pantoprazole was the most **stable** compound and **lansoprazole** the least **stable**. The stabilities of the compds. in salt solns. were in the following order: phosphate buffer < trisodium citrate < citrate buffer ≤ acetate buffer < citric acid ≤ monosodium citrate ≤ calcium carbonate < sodium bicarbonate < sodium chloride < **water**. The rate of degradation had a direct relationship with the H+ and salt concentration

ST salt stability **lansoprazole** HPLC detn; omeprazole stability salt HPLC detn; pantoprazole stability salt HPLC detn; chromatog liq drug stability salt detn

IT Buffers
(salts effect on stability of **lansoprazole** and omeprazole and pantoprazole determination by HPLC)

IT Salts, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(salts effect on stability of **lansoprazole** and omeprazole and pantoprazole determination by HPLC)

IT 73590-58-6, Omeprazole 102625-70-7, Pantoprazole 103577-45-3, **Lansoprazole**
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(salts effect on stability of **lansoprazole** and omeprazole and pantoprazole determination by HPLC)

IT 68-04-2, Trisodium citrate 77-92-9, Citric acid, biological studies 144-55-8, Carbonic acid monosodium salt, biological studies 471-34-1, Calcium carbonate, biological studies 7647-14-5, Sodium chloride, biological studies 18996-35-5, Monosodium citrate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(salts effect on stability of **lansoprazole** and omeprazole and pantoprazole determination by HPLC)

L2 ANSWER 22 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:605522 CAPLUS
DOCUMENT NUMBER: 125:230845
TITLE: New **stable** galenic formulations containing an acid-labile benzimidazole compound and their production
INVENTOR(S): Ballester Rodes, Montserrat; Van Boven, Marinus
PATENT ASSIGNEE(S): Esteve Quimica, S.A., Spain
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Spanish

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9623500	A1	19960808	WO 1996-ES13	19960126
W: AL, AM, AT, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, CZ, DE, DE, DK, DK, EE, EE, FI, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
ES 2094694	A1	19970116	ES 1995-181	19950201
ES 2094694	B1	19971216		
US 5626875	A	19970506	US 1995-429689	19950427
IL 116673	A1	20001031	IL 1996-116673	19960104
IN 186596	A	20011006	IN 1996-CA104	19960122
CA 2184842	AA	19960808	CA 1996-2184842	19960126
AU 9645403	A1	19960821	AU 1996-45403	19960126
EP 773025	A1	19970514	EP 1996-901349	19960126
EP 773025	B1	20000607		
R: AT, BE, CH, DE, DK, ES, FR, GB, IE, IT, LI, NL, PT, SE				
JP 09511257	T2	19971111	JP 1996-523278	19960126
EP 993830	A2	20000419	EP 1999-116334	19960126
EP 993830	A3	20011004		
EP 993830	B1	20050413		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, PT, IE, SI				
AT 193649	E	20000615	AT 1996-901349	19960126
ES 2148725	T3	20001016	ES 1996-901349	19960126
PT 773025	T	20001031	PT 1996-901349	19960126
DE 29623938	U1	20001109	DE 1996-29623938	19960126
TW 503115	B	20020921	TW 1996-85100946	19960126
AT 292967	E	20050415	AT 1999-116334	19960126
ZA 9600683	A	19970730	ZA 1996-683	19960130
FI 9603916	A	19960930	FI 1996-3916	19960930
PRIORITY APPLN. INFO.:			ES 1995-181 A	19950201
			EP 1996-901349 A3	19960126
			WO 1996-ES13 W	19960126
OTHER SOURCE(S):	MARPAT 125:230845			

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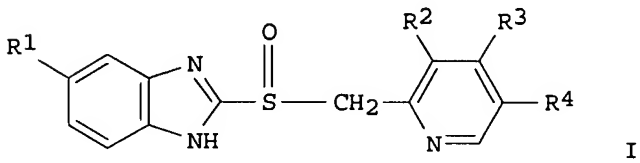


I

AB The title formulations comprise a neutral core on which is applied a layer containing the active ingredient (I; R1 = H, MeO, F2CHO; R2 = Me, MeO; R3 = MeO, F3CCH2O; R4 = H, Me), a **water**-soluble polymer, and nonalk. reaction vehicles; on this layer is applied a 2nd isolating layer which comprises a **water**-soluble polymer, a pigment, and talc, and a last enteric layer which contains a polymer, a plasticizer, and talc. Thus, 3010 g cores composed of sugar and starch were coated in a fluidized bed with a dispersion of omeprazole 436, hydroxypropylmethylcellulose 444, and talc 118 in H2O 3440 g. After drying, the pellets were coated with a

dispersion of hydroxypropylmethylcellulose 355, talc 43, and TiO2 43 in H2O 2365 g, dried, given an enteric coating of methacrylic acid copolymer 1950, tri-Et citrate 98, and talc 98 in H2O 1890 g, dried, and stored at 40° and 75% relative humidity. Pellets stored in glass containers showed little discoloration or loss of omeprazole after 3 mo.

TI New **stable** galenic formulations containing an acid-labile benzimidazole compound and their production

AB The title formulations comprise a neutral core on which is applied a layer containing the active ingredient (I; R1 = H, MeO, F2CHO; R2 = Me, MeO; R3 = MeO, F3CCH2O; R4 = H, Me), a **water**-soluble polymer, and nonalk. reaction vehicles; on this layer is applied a 2nd isolating layer which comprises a **water**-soluble polymer, a pigment, and talc, and a last enteric layer which contains a polymer, a plasticizer, and talc. Thus, 3010 g cores composed of sugar and starch were coated in a fluidized bed with a dispersion of omeprazole 436, hydroxypropylmethylcellulose 444, and talc 118 in H2O 3440 g. After drying, the pellets were coated with a dispersion of hydroxypropylmethylcellulose 355, talc 43, and TiO2 43 in H2O 2365 g, dried, given an enteric coating of methacrylic acid copolymer 1950, tri-Et citrate 98, and talc 98 in H2O 1890 g, dried, and stored at 40° and 75% relative humidity. Pellets stored in glass containers showed little discoloration or loss of omeprazole after 3 mo.

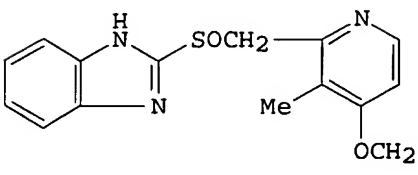
IT Ulcer inhibitors
(**stable** galenic formulations containing acid-labile benzimidazole compds.)

IT Pharmaceutical dosage forms
(pellets, enteric-coated, **stable** galenic formulations containing acid-labile benzimidazole compds.)

IT 73590-58-6, Omeprazole 103577-45-3, **Lansoprazole**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** galenic formulations containing acid-labile benzimidazole compds.)

IT 9004-64-2, Hydroxypropylcellulose 9004-65-3, Hydroxypropylmethylcellulose 25086-15-1, Methacrylic acid/methyl methacrylate copolymer
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stable** galenic formulations containing acid-labile benzimidazole compds.)

L2 ANSWER 23 OF 23 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:181047 CAPLUS
DOCUMENT NUMBER: 116:181047
TITLE: Formulation studies of an acid-unstable antiulcer drug, **lansoprazole**
AUTHOR(S): Hirai, Shinichiro
CORPORATE SOURCE: Res. Dev. Div., Takeda Chem. Ind., Ltd., Osaka, 532, Japan
SOURCE: Pharm Tech Japan (1992), 8(2), 213-19
CODEN: PTJAE9; ISSN: 0910-4739
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
GI



I

AB **Lansoprazole** (I), a new substituted benzimidazole, is a highly specific inhibitor of gastric (H+ + K+)-ATPase. Since this compound is practically insol. in **water** and unstable in the acidic conditions, it is necessary to design dosage forms for improving bioavailability. From the relationship between the gastric pH and the absorption, development of an enteric dosage form was necessary to protect the degradation in the stomach. Enteric granules had better absorption properties than an enteric tablet. Moreover, by the addition of MgCO3, as an alkaline stabilizer, and by the manufacturing method using a centrifugal fluid-bed granulator instead of an extruder-spheronizer, very **stable** enteric granules were obtained. Also, I capsule containing enteric granules showed good absorption properties in human.

TI Formulation studies of an acid-unstable antiulcer drug, **lansoprazole**

AB **Lansoprazole** (I), a new substituted benzimidazole, is a highly specific inhibitor of gastric (H+ + K+)-ATPase. Since this compound is practically insol. in **water** and unstable in the acidic conditions, it is necessary to design dosage forms for improving bioavailability. From the relationship between the gastric pH and the absorption, development of an enteric dosage form was necessary to protect the degradation in the stomach. Enteric granules had better absorption properties than an enteric tablet. Moreover, by the addition of MgCO3, as an alkaline stabilizer, and by the manufacturing method using a centrifugal fluid-bed granulator instead of an extruder-spheronizer, very **stable** enteric granules were obtained. Also, I capsule containing enteric granules showed good absorption properties in human.

ST **lansoprazole** enteric granule capsule

IT Gastric juice
(**lansoprazole** degradation in, enteric granules for protection against)

IT Drug bioavailability
(of **lansoprazole**, from enteric granules in capsules, in humans)

IT Pharmaceutical dosage forms
(capsules, containing **lansoprazole** enteric granules, formulation and evaluation of)

IT Granulation
(fluidized-bed, of **lansoprazole**, for enteric formulation)

IT Pharmaceutical dosage forms
(granules, enteric, of **lansoprazole**, formulation and evaluation of)

IT 103577-45-3, **Lansoprazole**
RL: BIOL (Biological study)
(capsules containing enteric granules of, formulation and evaluation of)

IT 546-93-0, Magnesium carbonate
RL: BIOL (Biological study)
(stabilizer, for **lansoprazole** enteric granules)

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